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L21 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:824882 HCAPLUS
DOCUMENT NUMBER: 141:319990
TITLE: Composite **scaffolds** seeded with mammalian cells
INVENTOR(S): Rezania, Alireza; Zimmerman, Mark
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004197375	A1	20041007	US 2003-405693	20030402
US 2004197367	A1	20041007	US 2003-727200	20031203
CA 2463443	AA	20041002	CA 2004-2463443	20040402
EP 1466633	A1	20041013	EP 2004-252019	20040402
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2004305748	A2	20041104	JP 2004-110328	20040402

PRIORITY APPLN. INFO.: US 2003-405693 A1 20030402
AB Implantable, biocompatible **scaffolds** containing a biocompatible, **porous**, polymeric matrix, a biocompatible, **porous**, fibrous mat encapsulated by and disposed within said polymeric matrix, and a plurality of mammalian cells seeded within said tissue **scaffold** are disclosed. The invention also is directed to **methods** of treating disease or structural defects in a mammal utilizing the **scaffolds** of the invention.

L21 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:822828 HCAPLUS
DOCUMENT NUMBER: 141:320154
TITLE: Intervertebral fusion implant with fusion cage made of **ceramic** or polymer
INVENTOR(S): Dimauro, Thomas M.; Serhan, Hassan
PATENT ASSIGNEE(S): Depuy Spine, Inc., USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1464307	A1	20041006	EP 2004-251928	20040331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-405062 A 20030331
AB An intervertebral fusion device, a **method** of making the intervertebral fusion device, and a **method** of using the intervertebral fusion device to promote fusion between two consecutive vertebrae in a patient is described. The intervertebral fusion device has an intervertebral fusion cage comprising (a) a a load bearing wall, and a **porous** matrix adjacent to the load bearing wall, and (b) one or

more agents that promote bone growth attached to the inner surface, e.g., a concentrated **growth factor.** The load bearing wall of the fusion cage has a greater d. than the internal **porous** matrix and is made of a **ceramic** or a polymer. The open pores of the **porous** matrix define an inner surface to which one or more agents that promote bone growth are attached, such as progenitor cells and **growth factors.**

L21 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:429563 HCAPLUS
DOCUMENT NUMBER: 141:59628
TITLE: A new high **porous** silica-sol-gel-**ceramics** for **bone grafting** - in-vivo long-time investigations
AUTHOR(S): Bienengraeber, V.; Gerber, Th.; Trykova, T.; Kundt, G.; Henkel, K.-O.
CORPORATE SOURCE: Klinik fuer Mund-Kiefer- und Plastische Gesichtschirurgie "Hans Moral", Universitaet Rostock, Rostock, Germany
SOURCE: Materialwissenschaft und Werkstofftechnik (2004), 35(4), 234-239
CODEN: MATWER; ISSN: 0933-5137
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The new **calcium phosphate ceramics** was produced by a sol-gel-process at 200 °Celsius with silica (SiO2) as adjuvant. The aim of this investigation was to test the **osteoinductive** effect of these **bioceramics** and to prove its biodegrdn. by animal expts. One year old minipigs were used and divided into 3 groups (n=6). Critical size defects (> 5cm3) in the mandible were filled by different materials (group 1: 60 % hydroxylapatite [HA] + 40 % β-tricalciumphosphate, group 2: only HA; group 3: control, without **ceramics**). Eight months later clin., histol., morpho-metrical and REM investigations concerning the state of former defected mandible were made. In groups 1 and 2 a complete reossification of the bone defects and a biodegrdn. rate of **ceramics** of more than 96 % were recognized. In conclusion silica-**calcium phosphate ceramics** made by a sol gel **method** seems to be suitable for filling bone defects in men and is of interest for orthopedic surgery, traumatol., craniomaxillofacial surgery and dentistry. Recently a clin. study was started.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:3713 HCAPLUS
DOCUMENT NUMBER: 140:65285
TITLE: Polymer-**bioceramic** composite for orthopedic applications and **method** of manufacture thereof
INVENTOR(S): King, Richard S.; Smith, Todd S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004002770	A1	20040101	US 2003-449058	20030602
EP 1374922	A1	20040102	EP 2003-254096	20030627

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: US 2002-392488P P 20020628

AB Polymer-**bioceramic** structures are described for use in the repair of bone defects. The composites of the present disclosure are characterized by a polymer disposed in a **porous** **bioceramic** matrix. Processes for preparing the composites of the present invention by compression molding are described, including compression molding to induce orientation of the polymer is multiple directions. The composites of the present invention are also useful as drug delivery vehicles to facilitate the repair of bone defects.

L21 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:855770 HCAPLUS
DOCUMENT NUMBER: 139:341729
TITLE: **Method** of manufacturing **hydroxyapatite** and uses therefor in delivery of nucleic acids
INVENTOR(S): Kumta, Prashant N.; Sfeir, Charles; Hollinger, Jeffrey; Choi, Daiwon; Weiss, Lee; Campbell, Phil
PATENT ASSIGNEE(S): Carnegie Mellon University, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088925	A2	20031030	WO 2003-US8450	20030319
WO 2003088925	A3	20031211		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003219466	A1	20031127	US 2003-393507	20030319

PRIORITY APPLN. INFO.: US 2002-373494P P 20020418

AB Provided is a **method** for production of nanocryst. **hydroxyapatite** particles, and nanocryst. **hydroxyapatite** particles produced according to the **method.** The nanocryst. **hydroxyapatite** particles exhibit substantially superior cell transformation abilities as compared to known and com.-available **calcium phosphate** kits. The nanocryst. **hydroxyapatite** particles also find use in tissue engineering applications, for example bone and tooth engineering and repair applications.

L21 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:757080 HCAPLUS

DOCUMENT NUMBER: 139:281302
TITLE: **Porous** beta-**tricalcium** **phosphate** granules and **methods** for producing same
INVENTOR(S): Dalal, Paresh S.; Dimaano, Godofredo R.; Toth, Carol Ann; Kulkarni, Shailesh C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 64 pp., Cont.-in-part of U.S. Ser. No. 798,518.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003180376	A1	20030925	US 2001-960789	20010921
US 2003049328	A1	20030313	US 2001-798518	20010302
CA 2439813	AA	20020912	CA 2002-2439813	20020226
WO 2002070029	A2	20020912	WO 2002-US5827	20020226
WO 2002070029	A3	20030206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1372748	A2	20040102	EP 2002-748362	20020226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004262758	A2	20040924	JP 2004-173260	20040610

PRIORITY APPLN. INFO.:

US 2001-798518	A2	20010302
US 2001-960789	A	20010921
JP 2002-569200	A3	20020226
WO 2002-US5827	W	20020226

AB A **porous** β- **tricalcium** **phosphate** material for bone implantation is provided. The multiple pores in the **porous** TCP body are sep. discrete voids and are not interconnected. The pore size diameter is in the range of 20-500 μm, preferably 50-125 μm. The **porous** β-TCP material provides a carrier matrix for bioactive agents and can form a moldable putty composition upon the addition of a binder. Preferably, the bioactive agent is encapsulated in a biodegradable agent. The invention provides a kit and an implant device comprising the **porous** β-TCP, and a bioactive agent and a binder. The invention also provides an implantable prosthetic device comprising a prosthetic implant having a surface region, a **porous** β-TCP material disposed on the surface region and optionally comprising at least a bioactive agent or a binder. **Methods** of producing the **porous** β-TCP material and inducing bone formation are also provided.

L21 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:633417 HCAPLUS
DOCUMENT NUMBER: 139:169389

TITLE: Bioresorbable osteoconductive compositions for bone regeneration
INVENTOR(S): Wise, Donald L.; Trantolo, Debra J.; Lewandrowski, Kai-Uwe; Gresser, Joseph D.
PATENT ASSIGNEE(S): Cambridge Scientific, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003065996	A2	20030814	WO 2003-US3567	20030205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003180344	A1	20030925	US 2003-359445	20030205
PRIORITY APPLN. INFO.:			US 2002-354833P P	20020205

AB Bioresorbable osteoconductive compns. and **methods** of using the composition as a **scaffold** for bone repair in periodontal, alveolar or maxillary regeneration, bony cranial defects, and spinal regeneration are disclosed. The bioresorbable compns. contain a bioresorbable polymer, a micro or nano particulate filler and a pore creating substance. The bioresorbable polymer can be electronically unsatd. and crosslinkable with a crosslinking agent. The micro or nano filler can be any natural biocompatible material such as a metals, calcium carbonate, carbon, a biocompatible synthetic material, or a **bioceramics** such as **hydroxyapatite.** The pore creating substance can be an effervescent agent such as a carbonate and an acid. Nano- or micro-**hydroxyapatite** particulated augments poly(propylene fumarate) **bone grafts.**

L21 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:29538 HCAPLUS
DOCUMENT NUMBER: 138:78546
TITLE: Material and **method** for cranial bone restoration using **porous calcium phosphates** and bioabsorbable or biocompatible covering materials
INVENTOR(S): Inoue, Akira; Irie, Hiroyuki
PATENT ASSIGNEE(S): Olympus Optical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003010310	A2	20030114	JP 2001-195221	20010627

PRIORITY APPLN. INFO.: JP 2001-195221 20010627

AB The materials, which restore defective parts or gaps formed between skull and resected bone piece during craniotomy, comprise (a) **porous** body or **porous** particles of **Ca phosphate** which show porosity 50-90%, have continuous pores having pore diameter 50-1000 μm and those having pore diameter ≤5 μm, and fill the defective parts or gaps and (b) bioabsorbable organic materials or biocompatible materials such as fibrins, poly(lactic acid), collagen, hyaluronic acid, etc., which cover the **porous** body or particles applied to the defects or gaps. The **Ca phosphate** **porous** body or particles may be composites with ≥1 animal **growth factors** selected from **BMP**, FGF, TGF-β, IGF, PDGF, and VEGF. The materials promote bone healing and prevent postoperative depression.

L21 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:695831 HCAPLUS
DOCUMENT NUMBER: 137:237785
TITLE: **Porous** beta-**tricalcium** **phosphate** granules for bone implantation, and **methods** for producing same
INVENTOR(S): Dalal, Paresh S.; Dimaano, Godofredo R.; Toth, Carol Ann; Kulkarni, Shailesh C.
PATENT ASSIGNEE(S): Stryker Corporation, USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070029	A2	20020912	WO 2002-US5827	20020226
WO 2002070029	A3	20030206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003049328	A1	20030313	US 2001-798518	20010302
US 2003180376	A1	20030925	US 2001-960789	20010921
CA 2439813	AA	20020912	CA 2002-2439813	20020226
EP 1372748	A2	20040102	EP 2002-748362	20020226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:
US 2001-798518 A 20010302
US 2001-960789 A 20010921
WO 2002-US5827 W 20020226

AB A **porous** β- **tricalcium phosphate** material for bone implantation is provided. The multiple pores in the **porous** TCP body are sep. discrete voids and are not interconnected. The pore size diameter is in the range of 20-500 μm, preferably 50-125 μm. The **porous** β-TCP material provides a carrier matrix for bioactive agents and can form a moldable

putty composition upon the addition of a binder. Preferably, the bioactive agent is encapsulated in a biodegradable agent. The invention provides a kit and an implant device comprising the **porous** β-TCP, and a bioactive agent and a binder. The invention also provides an implementable prosthetic device comprising a prosthetic implant having a surface region, a **porous** β-TCP material disposed on the surface region optionally comprising at least a bioactive agent or a binder. **Methods** of producing the **porous** β-TCP material and including bone formation are also provided.

L21 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:574971 HCAPLUS
DOCUMENT NUMBER: 137:129946
TITLE: Injectable **porous bone graft** materials
INVENTOR(S): Wironen, John F.
PATENT ASSIGNEE(S): Regeneration Technologies, Inc., USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058755	A2	20020801	WO 2002-US3092	20020125
WO 2002058755	A3	20030227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2436162	AA	20020801	CA 2002-2436162	20020125
EP 1359951	A2	20031112	EP 2002-720893	20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004533276	T2	20041104	JP 2002-559088	20020125

PRIORITY APPLN. INFO.:
US 2001-263972P P 20010125
WO 2002-US3092 W 20020125

AB A bone-like implant capable of increasing its porosity in situ comprising at least one bone-like compound, e.g. phosphates, with at least one hydrophobic carrier or a degradable component. The bone-like implant includes its manufacture and **methods** of use. One aspect of the bone-like implant is to provide a **method** of repairing a bone defect or related injuries. The bone-like implant includes several embodiments capable of increasing its porosity in situ (no data).

L21 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:157554 HCAPLUS
DOCUMENT NUMBER: 136:205417
TITLE: A **porous** carrier for controlled drug release
INVENTOR(S): Sambrook, Rodney Martin; Austin, Wayne; Sambrook, Mark Rodney; Hannon, Michael
PATENT ASSIGNEE(S): Dytech Corporation Ltd., UK

SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015881	A2	20020228	WO 2001-GB3739	20010821
WO 2002015881	A3	20020627		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2420194	AA	20020228	CA 2001-2420194	20010821
AU 2001079970	A5	20020304	AU 2001-79970	20010821
EP 1311241	A2	20030521	EP 2001-958246	20010821
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004506679	T2	20040304	JP 2002-520790	20010821
BR 2001013429	A	20040406	BR 2001-13429	20010821
US 2004265350	A1	20041230	US 2003-728006	20031203
PRIORITY APPLN. INFO.:			GB 2000-20610 A	20000821
			WO 2001-GB3739 W	20010821
			US 2003-362314 B1	20030220

AB A **porous** carrier having interconnected porosity is loaded with a drug or other material for controlled release of the drug or other material. Using a vacuum **method** cisplatin in an aqueous sodium chloride solution was injected onto an hydroxylapatite block of porosity 84.04%. After drying patches of yellow presumed to be cisplatin were observed on the surface of the block. No yellow color was observed within the block. Release of cisplatin was rapid, with almost the entire drug being released after 45 min. The fast release of the drug may indicate that penetration into the block is not occurring and the drug is merely being released from the surface of the block.

L21 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:906235 HCAPLUS
DOCUMENT NUMBER: 136:25166
TITLE: **Method** for composite cell-based implants using mineral or polymeric microcarriers
INVENTOR(S): Frondoza, Carmelita G.; Hungerford, David S.; Shikani, Alan H.; Domb, Abraham J.; Fink, David J.; Bloom, Leonard
PATENT ASSIGNEE(S): Chondros, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U. S. Ser. No. 825,632.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2001051834	A1	20011213	US 2001-922909	20010806
US 2001014475	A1	20010816	US 2001-825632	20010404
US 2002012705	A1	20020131	US 2001-929697	20010814
US 6514522	B2	20030204		
US 2002123142	A1	20020905	US 2002-39718	20020103
US 2002133235	A1	20020919	US 2002-66992	20020204
US 2004117033	A1	20040617	US 2003-731366	20031209

PRIORITY APPLN. INFO.:

US 1998-81016P	P	19980408
US 1998-104842P	P	19981020
US 1999-275319	A2	19990324
US 2000-712662	A2	20001114
US 2001-825632	A2	20010404
US 1999-165608P	P	19991115
US 2000-228855P	P	20000829
US 2001-922909	A3	20010806

AB This invention is a **method** for the implantation of a combination of cells or cell-microcarrier aggregates wherein one component comprises a solid implantable construct and a second component comprises an injectable formulation. For example, in one embodiment, the solid implant may be first implanted to fill the majority of the cavity receiving the implant, and then cells or cell-microcarrier aggregates in an injectable format, with or without the addition of gelling materials to promote rapid gelling in situ, may be injected into spaces surrounding the solid implant in order to secure the solid implant in the site and/or to promote rapid adherence and/or integration of the solid implant to surrounding tissues. Also contemplated in this embodiment is that the cellular composition of the injectable component may differ from that of the solid component. For example, the solid implant may result from the culturing of chondrocytes on microcarriers or **scaffolds**, e.g., calcium carbonate, **calcium phosphate** or calcium sulfate, biopolymers, or synthetic polymers such as polylactic acid, polyglycolic or their **copolymers**, thereby resulting in an implant having cartilage-like properties, whereas the injectable cells or aggregates may result from the culturing of stem cells, resulting thereby in cells capable of producing cells of a chondrogenic, fibroblastic, myoblastic or osteoblastic phenotype. In this example, cells in the injectable aggregates may promote the fixation to or rapid integration of the solid cartilage implant into surrounding cartilage, connective tissue, muscle or bone, resp. A **method** of treating a skin lesion or nose or ear defects comprises filling the lesion or defect with a solid cell-containing implant along with an injectable cell-containing formulation.

L21 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:73537 HCAPLUS
DOCUMENT NUMBER: 134:136750
TITLE: Compositions with enhanced osteogenic potential, **methods** for making the same and uses thereof
INVENTOR(S): Chen, Charles C.; Jefferies, Steven R.
PATENT ASSIGNEE(S): GenSci Orthobiologics, Inc., USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,707,962.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6180606	B1	20010130	US 1998-6583	19980113

US 5707962	A	19980113	US 1994-312091	19940928
US 6180605	B1	20010130	US 1998-2674	19980105
US 2001014667	A1	20010816	US 2001-833660	20010417
PRIORITY APPLN. INFO.:			US 1994-312091	A2 19940928
			US 1998-2674	A2 19980105
			US 2001-772512	A1 20010129

AB Disclosed are osteogenic compns., and **methods** for preparing same, which compns. comprise a **porous** or semi-**porous** matrix, an osteogenic factor and an agent such as **growth factors**, nutrient factors, drugs, calcium-containing compds., blood products, large mol. weight proteins, or combinations thereof. These materials can be used in a wide range of clin. procedures to replace and restore osseous or periodontal defects. An osteogenic collagen sponge was fabricated from pulverized tendon collagen powder, demineralized bone particles, and lyophilized **bone morphogenetic** protein (RMP).

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:553459 HCAPLUS
DOCUMENT NUMBER: 133:155511
TITLE: Highly-mineralized osteogenic sponge compositions, and uses thereof
INVENTOR(S): McKay, William F.
PATENT ASSIGNEE(S): SDGI Holdings, Inc., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045871	A1	20000810	WO 2000-US3043	20000204
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2362049	AA	20000810	CA 2000-2362049	20000204
EP 1150726	A1	20011107	EP 2000-905989	20000204
EP 1150726	B1	20031105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002536077	T2	20021029	JP 2000-596990	20000204
AT 253385	E	20031115	AT 2000-905989	20000204
AU 772682	B2	20040506	AU 2000-27568	20000204
ES 2209820	T3	20040701	ES 2000-905989	20000204
PRIORITY APPLN. INFO.:			US 1999-118615P	P 19990204
			WO 2000-US3043	W 20000204

AB Osteogenic sponge compns. having enhanced **osteoinductive** properties for use in bone repair are described. The compns. include a quickly resorbable **porous** carrier, a more slowly resorbed mineral **scaffold** and an osteogenic factor, preferably a **bone morphogenetic** protein. The compns. enable

increased **osteoinductive** activity while retaining a reliable **scaffold** for the formation of new bone at an implant site. **Methods** for therapeutic use of the compns. are also described.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:553458 HCAPLUS
DOCUMENT NUMBER: 133:155510
TITLE: Osteogenic paste compositions and uses thereof
INVENTOR(S): McKay, William F.
PATENT ASSIGNEE(S): SDGI Holdings, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000045870	A1	20000810	WO 2000-US3024		20000204
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2362046	AA	20000810	CA 2000-2362046		20000204
EP 1150725	A1	20011107	EP 2000-905983		20000204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002536076	T2	20021029	JP 2000-596989		20000204
AU 770196	B2	20040212	AU 2000-27564		20000204
US 2004002558	A1	20040101	US 2001-923117		20010806
PRIORITY APPLN. INFO.:			US 1999-118614P	P	19990204
			WO 2000-US3024	W	20000204

AB Described are osteogenic paste compns. with enhanced **osteoinductive** properties for use in bone repair. Compns. comprising a quickly resorbable paste carrier, a more slowly resorbed mineral matrix, and **Bone Morphogenetic** Protein (**BMP**) or other osteogenic factor are described which enable increased **osteoinductive** activity while retaining a reliable **scaffold** for the formation of new bone at the implant site. **Methods** for making and **methods** for therapeutic use of the compns. are also disclosed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:736893 HCAPLUS
DOCUMENT NUMBER: 131:332976
TITLE: Sustained dna delivery from structural **porous** matrices for gene therapy applications with special emphasis is on bone formation and regeneration
INVENTOR(S): Shea, Lonnie D.; Bonadido, Jeffrey; Mooney, David J.
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA

SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958656	A2	19991118	WO 1999-US10330	19990512
WO 9958656	A3	20000106		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BJ, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9938986	A1	19991129	AU 1999-38986	19990512

PRIORITY APPLN. INFO.:

US 1998-85305P	P	19980513
US 1998-109054P	P	19981119
WO 1999-US10330	W	19990512

AB Disclosed are particular 3-dimensional structural matrixes containing DNA and their use in the prolonged release of DNA in various biol. environments. The structural matrix is a **porous** polymer [PLGA]-based containing pores formed by gas foaming involving inert gases (CO2) and leaching out of a water-soluble particulate (salt, NACL, sugar, glucose, sucrose, mannitol) when exposed to body fluids. The admixt. is compression molded into a selected size and shape prior to executing the gas foaming process. The structural matrix may also be an alginate or modified alginate matrix. This structural matrix is a biocompatible or biodegradable matrix. It may also be a lactic acid polymer, glycolic acid polymer or lactic acid/glycolic acid **copolymer** matrix. At least part of this matrix may be comprised of lactic acid/glycolic acid (PLGA) **copolymer** matrix. The structural matrix may be modified where one side section is bonded to one cell interaction mol. such as cell adhesion mols., cell attachment peptides, proteoglycan attachment peptide sequences, proteoglycans, cell adhesion polysaccharides, **growth factors**, cell adhesion enzymes, RGD peptide, fibronectin, vitronectin, Laminin A, Laminin B1, Laminin B2, collagen 1 and thrombospondin. The DNA-matrix materials are created such that they maintain a defined space, allowing cellular migration, transfection and proliferation to occur in a controlled manner. Such DNA-containing structural matrixes are thus particularly useful in in vivo cell transfection and gene expression in the context of gene therapy. This may encode a protein for stimulating bone progenitors or wound healing in fibroblast or in tissue or organ regeneration or transplantation or an antigen for immunity or cytotoxic or apoptosis-inducing protein or a transcription factor or elongation factor or cell cycle control protein or kinase or phosphatase or DNA repair protein or oncogene or tumor suppressor or angiogenic protein or anti-angiogenic protein or immune response stimulating protein or cell surface receptor or accessory signaling mol. or transport protein or anti-**bacterial** or anti-**viral** protein or **hormone** or neurotransmitter or **growth factor** or **growth factor** receptor or interferon or interleukin or chemokine or cytokine or colony stimulating factor or chemotactic factor protein of growth **hormone** or parathyroid **hormone** or PTH1-34 **polypeptide** or **bone morphogenic** protein or **BMP**-2A or **BMP**-2B or **BMP**-3 or

BMP-4 or **BMP**-5 or **BMP**-6 or **BMP**-7 or **BMP**-8 or TGF-α or TGF-β1 or TGF-β2 or latent TGFβ binding protein or activin/inhibin protein or FGF or GMCSF or EGF or PDGF or insulin-like **growth factor** or leukemia inhibitory factor. This **method** allows for the use in gene transfer to cells within a tissue site and in manufacture of a medicament for gene therapy. Implantable medical devices comprising this gene-matrix are described. The release of nucleic acids from the matrix is controlled by diffusion. This **method** also applies to cancer therapy or treating **viral** infection.

L21 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:636052 HCAPLUS
DOCUMENT NUMBER: 131:253369
TITLE: In vivo gene transfer **methods** for wound healing
INVENTOR(S): Goldstein, Steven A.; Bonadio, Jeffrey
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 316,650.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5962427	A	19991005	US 1996-631334	19960412
US 5763416	A	19980609	US 1994-199780	19940218
US 5942496	A	19990824	US 1994-316650	19940930
WO 9522611	A2	19950824	WO 1995-US2251	19950221
WO 9522611	A3	19960208		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2251655	AA	19971023	CA 1997-2251655	19970411
WO 9738729	A1	19971023	WO 1997-US7301	19970411
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9728212	A1	19971107	AU 1997-28212	19970411
AU 710386	B2	19990916		
EP 892644	A1	19990127	EP 1997-922578	19970411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1226835	A	19990825	CN 1997-195326	19970411
RU 2170104	C2	20010710	RU 1998-120477	19970411
JP 2001519767	T2	20011023	JP 1997-537463	19970411
NO 9804729	A	19981214	NO 1998-4729	19981009
KR 2000005376	A	20000125	KR 1998-708098	19981012
PRIORITY APPLN. INFO.:			US 1994-199780	A2 19940218
			US 1994-316650	A2 19940930

WO 1995-US2251	A2	19950221
US 1996-631334	A	19960412
WO 1997-US7301	W	19970411

AB The present invention relates to an in vivo **method** for specific targeting and transfer of DNA into mammalian repair cells. The **method** involves implanting a matrix containing DNA of interest into a fresh wound site, wherein the matrix acts as a **scaffolding** that promotes cell growth, and in turn, gene transfer. Repair cells, which normally originate in viable tissue surrounding the wound, proliferate and migrate into the gene activated matrix, wherein they encounter, take up, and express the DNA. Transfected repair cells, therefor act as in situ bioreactors which produce DNA-encoded agents that heal the wound. The transferred DNA may include any DNA encoding a therapeutic protein of interest. The invention further relates to pharmaceutical compns. that may be used in the practice of the invention to transfer the DNA of interest.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:555421 HCAPLUS
DOCUMENT NUMBER: 132:112999
TITLE: Evaluation of human recombinant **bone morphogenetic** protein-2-loaded **tricalcium phosphate** implants in rabbits' bone defects
AUTHOR(S): Laffargue, Ph.; Hildebrand, H. F.; Rtaimate, M.; Frayssinet, P.; Amoureux, J. P.; Marchandise, X.
CORPORATE SOURCE: Laboratoire de Biophysique, Unite Programmee de Recherche et d'Enseignement Scientifique, Equipe d'Accueil (UPRES EA) 1049, Faculte de Medecine, Lille, Fr.
SOURCE: Bone (New York) (1999), 25(2, Suppl.), 55S-58S
CODEN: BONEDL; ISSN: 8756-3282
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Porous** β- **tricalcium phosphate** (βTCP) has osteoconductive properties. The adsorption of human recombinant **bone morphogenetic** protein-2 (rhBMP-2) onto TCP could realize an **osteoinductive** bone substitute. We evaluated it on an animal model by dual-energy x-ray absorptiometry (DEXA) and solid-state 31P-NMR spectroscopy. βTCP cylinders loaded with rhBMP-2 were implanted into rabbits' femoral condyle bone defects, and βTCP alone as control into the contralateral femur. We studied 2 different doses of rhBMP-2 (10 and 40 μg) on 2 groups of 4 animals. Evaluation consisted in radiog., histol., and histomorphometry, DEXA, and NMR spectroscopy using an original **method** of quantification. With both doses of rhBMP-2, we observed on radiographs an increase of trabecular bone around implants. Histol. showed resorption of the **ceramic**, trabecular bone with osteoblasts and osteoid substance around the implants, and colonization inside the **porous** βTCP by new bone formed. Histomorphometry showed that the osteoid surface (OS/BS) was greatest with the high dose of rhBMP-2. The difference was slight between the low dose of rhBMP-2 and control. DEXA showed a dose-dependent increase of bone mineral d. of rhBMP-2-loaded βTCP vs. control. NMR spectroscopy confirmed that the amount of new bone formed in βTCP was greater when βTCP carried rhBMP-2, and increased with the dose of rhBMP-2 used. βTCP was a good matrix for rhBMP-2, which gave it **osteoinductive** properties in an

orthotopic site, in a dose-dependent manner. Thus, such composite biomaterial seems to be of great interest in reconstructive bone surgery. Further studies are needed in clin. practice to determine optimal doses.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:139944 HCAPLUS
DOCUMENT NUMBER: 130:200967
TITLE: Three-dimensional polymer matrixes for tissue engineering and various applications
INVENTOR(S): Shastri, Venkatram R.; Martin, Ivan; Langer, Robert S.; Seidel, Joachim
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909149	A1	19990225	WO 1998-US16020	19980731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886810	A1	19990308	AU 1998-86810	19980731
US 6471993	B1	20021029	US 2000-463709	20000128

PRIORITY APPLN. INFO.:

US 1997-904780	A2	19970801
US 1997-67234P	P	19971202
US 1997-69547P	P	19971212
WO 1998-US16020	W	19980731

AB Matrixes that include a macrostructure having a semi-solid network and voids, and a microstructure having voids, in which the microstructure is located within the semi-solid network are disclosed. **Methods** for preparing these matrixes are also disclosed. The **porous** matrixes are useful in a variety of applications, including tissue engineering, electromagnetic shielding, and fuel cell applications. Lactic acid-glycolic acid **copolymer** was ground and mixed with methylene chloride to form a viscous paste, to which paraffin particles were added. The obtained homogeneous mixture was packed into a Teflon mold. The mold was then placed in a beaker containing hexane to extract the porogen. The mold was removed from the hexane and the matrix was removed from the mold. The matrix was air-dried, then lyophilized.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:527959 HCAPLUS
TITLE: Polymer based tissue engineering of bone
AUTHOR(S): Laurencin, Cato T.; Borden, Mark D.; Ambrosio, Archel A.; Attawia, Mohamed A.; Ko, Frank K.; Allcock, Harry R.; Morrill, Gina M.

CORPORATE SOURCE: Department Orthopaedic Surgery, Allegheny University the Health Sciences, Philadelphia, PA, 19129, USA
SOURCE: Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (1998), POLY-246. American Chemical Society: Washington, D. C.
CODEN: 66KYA2
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB The need for a synthetic alternative to conventional **bone grafts** stems from donor-site morbidity and limited supply. Using a tissue engineering approach, these replacements can be designed to provide the defect site with a temporary **scaffold** for bone regeneration while mech. supporting the surrounding tissue. This can be accomplished by fabricating **porous** matrixes from biodegradable materials such as degradable polyphosphazenes and polyesters. Our lab has conducted several studies indicating the feasibility of these two types of polymers as orthopaedic biomaterials. In vitro expts. have shown the growth, proliferation and phenotypic expression of osteoblasts on polyphosphazenes bearing amino acid ester side groups and on poly(lactide-co-glycolide) -- polymers which hydrolyze to metabolically benign products. Further in vivo work, showed that these biomaterials elicit a minimal **inflammatory** response and are capable of supporting bone growth. Using the **copolymer** poly(lactide-co-glycolide) [PLAGA] and **ceramic** **hydroxyapatite** [HA], we have also developed several **methods** for fabricating **porous** matrixes with mech. properties similar to trabecular bone: 1) the **sintered** microsphere **method** 2) the solvent cast microsphere **method** and 3) the gel microsphere **method.** Matrix porosity was the result of the random packing of polymer microspheres. SEM image anal. indicated a three-dimensional pore network and range in porosity from 21% to 50%. Mech. characterization indicated that all matrixes had a modulus within the range of trabecular bone (10 MPa - 2000 MPa).

L21 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:594654 HCAPLUS
DOCUMENT NUMBER: 127:253232
TITLE: An osteogenic device and a **method** for preparing the device
INVENTOR(S): Lindholm, T. Sam; Mattinen, Aulis
PATENT ASSIGNEE(S): Lindholm, T. Sam, Finland; Mattinen, Aulis
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731661	A1	19970904	WO 1996-FI118	19960229

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9647216	A1	19970916	AU 1996-47216	19960229
EP 883410	A1	19981216	EP 1996-903037	19960229
EP 883410	B1	20040818		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 273723	E	20040915	AT 1996-903037	19960229
FI 9801818	A	19981012	FI 1998-1818	19980825
PRIORITY APPLN. INFO.:			WO 1996-FI118 W	19960229

AB The present invention is related to an osteogenic device and its preparation Said device comprises a **bone morphogenetic** protein (**BMP**), preferably a modified **BMP** complex obtainable by a modification of the conventional guanidine hydrochloride extraction **method** and collagens, preferably collagen I or collagen IV, impregnated in and/or adsorbed on a **bioceramic** carrier, preferably a shapable body (block) originating from a coral skeleton. The **method** of isolating said modified **BMP** complex which lacks an immunogenic component and consists essentially of a 100-700 kD and a 15-25 kD protein with **osteoinductive** properties and preferably of the 15-25 kD protein which has improved storage properties as well as its use in the osteogenic device with improved **osteoinductive** properties is also disclosed.

L21 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1996:62313 HCAPLUS
DOCUMENT NUMBER:	124:185439
TITLE:	In-vivo evaluation of **porous** Ca2P2O7 with sodium phosphate addition in orthopedics
AUTHOR(S):	Lin, F.H.; Lin, C.C.; Liu, H.C.; Wang, C.Y.
CORPORATE SOURCE:	College of Medicine, National Taiwan University, Taipei, Taiwan
SOURCE:	Key Engineering Materials (1996), 115, 191-208 CODEN: KEMAEY; ISSN: 1013-9826
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The ultimate goal of implantation of biomaterials in the skeleton is to reach full integration of non-living implant with living bone. The material could be used, much as a **bone graft**, as material itself resorbs or dissolves as bone growth occurs, and end result is new remolded bone. Ca2P2O7 is one of intermediate product of bone mineralized crystal from amorphous **calcium phosphates.** The Ca2P2O7 doped with certain amount of Na4P2O7·10H2O was prepared as the developed material. In this study, the Na4P2O7·10H2O was used for liquid phase **sintering** additive which was expected to improve **sintering** process and promote physiol. bioresorbability. Compressive strength and 4-point bending strength were measured by Bionix test system 858. At the beginning, the mech. strength was proportionally increasing with the addition of Na4P2O7·10H2O up to 5 wt%, but thereafter decreased. The microstructure and crystalline identification was analyzed by the **techniques** of SEM, EPMA, TEM and XRD. The relationship between mech. strength of the **sintered bioceramics** and Na4P2O7·10H2O dopant was in terms of the presence of NaCa(PO3)3, grain growth and abnormal grain coalescence while dopant increased. Preliminary in-vivo evaluation was studied by rabbit femur condyle implantation model. There was no **inflammation** or any toxic sign during the exptl. period. The histol. section of intraosseous implantation revealed that the new bone directly deposited on the surface of the material at the 4th week after operation. The materials were gradually decreasing in volume and being replaced by the surrounding regenerated bone in the rabbit condyle in-vivo environment. The results encouraged us to conclude that the developed material did have a great potential as an ideal biodegradable bone substitute.

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L23 ANSWER 1 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004404949 EMBASE
TITLE: Bone tissue engineering: State of the art and future trends.
AUTHOR: Salgado A.J.; Coutinho O.P.; Reis R.L.
CORPORATE SOURCE: A.J. Salgado, 3B's Research Group, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal. asalgado@dep.uminho.pt
SOURCE: Macromolecular Bioscience, (9 Aug 2004) 4/8 (743-765). Refs: 308
ISSN: 1616-5187 CODEN: MBAIBU
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although several major progresses have been introduced in the field of bone regenerative medicine during the years, current therapies, such as **bone grafts**, still have many limitations. Moreover, and in spite of the fact that material science technology has resulted in clear improvements in the field of bone substitution medicine, no adequate bone substitute has been developed and hence large bone defects/injuries still represent a major challenge for orthopaedic and reconstructive surgeons. It is in this context that TE has been emerging as a valid approach to the current therapies for bone regeneration/substitution. In contrast to classic biomaterial approach, TE is based on the understanding of tissue formation and regeneration, and aims to induce new functional tissues, rather than just to implant new spare parts. The present review pretends to give an exhaustive overview on all components needed for making bone tissue engineering a successful therapy. It begins by giving the reader a brief background on bone biology, followed by an exhaustive description of all the relevant components on bone TE, going from materials to **scaffolds** and from cells to tissue engineering strategies, that will lead to "engineered" bone.

L23 ANSWER 2 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:405015 BIOSIS
DOCUMENT NUMBER: PREV200400409264
TITLE: A new bone-inducing biodegradable **porous** beta-**tricalcium phosphate.**
AUTHOR(S): Matsushita, Naofumi; Terai, Hidetomi [Reprint Author]; Okada, Takao; Nozaki, Kazutoshi; Inoue, Hikaru; Miyarnoto, Shimpei; Takaoka, Kunio
CORPORATE SOURCE: Sch MedDept Orthopaed SurgAbeno Ku, Osaka City Univ, 1-4-3 Asahi Machi, Osaka, 5458585, Japan hterai@med.osaka-cu.ac.jp
SOURCE: Journal of Biomedical Materials Research, (September 1 2004) Vol. 70A, No. 3, pp. 450-458. print.
ISSN: 0021-9304 (ISSN print).

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Oct 2004
Last Updated on STN: 20 Oct 2004

AB A new type of degradable biomaterial with bone-inducing capacity was made by combining **porous** beta-**tricalcium phosphate** (beta-TCP) with a delivery system for recombinant human **bone morphogenetic** protein-2 (rhBMP-2). The **BMP** delivery system consisted of a block **copolymer** composed of poly-D,L-lactic acid with random insertion of p-dioxanone and polyethylene glycol (PLA-DX-PEG), a known biocompatible and biodegradable material. The efficacy of this biomaterial in terms of its bone-inducing capacity was examined by ectopic bone formation in the dorsal muscles of the mouse. In the beta-TCP implants coated with the PLA-DX-PEG polymer containing more than 0.0025% (w/w) of rhBMP-2, new ectopic bone tissues with marrow were consistently found on the surface of implants. The radio-graphic density of beta-TCP was diminished in a time-dependent manner. On histological examination, numerous multinucleated osteoclasts with positive tartrate-resistant acid-phosphatase (TRAP) staining were noted on the surface of the beta-TCP. These experimental results indicate that beta-TCP implants coated with synthetic rhBMP-2 delivery system might provide effective artificial **bone-graft** substitutes with **osteoinductive** capacity and biodegradable properties. In addition, this type of biomaterial may require less rhBMP-2 to induce significant new bone mass. Copyright 2004 Wiley Periodicals, Inc.

L23 ANSWER 3 OF 43 MEDLINE on STN
ACCESSION NUMBER: 2004387987 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14730438
TITLE: Anterior lumbar interbody fusion with carbon fiber cage loaded with **bioceramics** and platelet-rich plasma. An experimental study on pigs.
AUTHOR: Li Haisheng; Zou Xuenong; Xue Qingyun; Egund Niels; Lind Martin; Bunger Cody
CORPORATE SOURCE: Orthopaedic Research Laboratory, Orthopaedic Department E, Aarhus University Hospital, Norrebrogade 44, 8000 Aarhus C, Denmark.. haisheng.li@iekf.au.dk
SOURCE: European spine journal : official publication of the European Spine Society, European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society, (2004 Jul) 13 (4) 354-8.
Journal code: 9301980. ISSN: 0940-6719.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040805
Last Updated on STN: 20041219
Entered Medline: 20041119

AB Platelet-rich plasma (PRP) is an autogenous source of **growth factor** and has been shown to enhance bone healing both in clinical and experimental studies. PRP in combination with **porous hydroxyapatite** has been shown to increase the bone ingrowth in a bone chamber rat model. The present study investigated whether the combination of beta **tricalcium phosphate** (beta-TCP) and PRP may enhance spinal fusion in a controlled animal study. Ten Danish Landrace pigs were used as a spinal fusion model. Immediately prior to the surgery, 55 ml blood was collected from each pig for processing PRP. Three-level anterior lumbar interbody fusion was

performed with carbon fiber cages and staples on each pig. Autogenous **bone graft**, beta-TCP, and beta-TCP loaded with PRP were randomly assigned to each level. Pigs were killed at the end of the third month. Fusion was evaluated by radiographs, CT scanning, and histomorphometric analysis. All ten pigs survived the surgery. Platelet concentration increased 4.4-fold after processing. Radiograph examination showed 70% (7/10) fusion rate in the autograft level. All the levels with beta-TCP+PRP showed partial fusion, while beta-TCP alone levels had six partial fusions and four non-fusions (P=0.08). CT evaluation of fusion rate demonstrated fusion in 50% (5/10) of the autograft levels. Only partial fusion was seen at beta-TCP levels and beta-TCP+PRP levels. Histomorphometric evaluation found no difference between beta-TCP and beta-TCP+PRP levels on new bone volume, remaining beta-TCP particles, and bone marrow and fibrous tissue volume, while the same parameters differ significantly when compared with autogenous **bone graft** levels. We concluded from our results in pigs that the PRP of the concentration we used did not improve the bone-forming capacity of beta-TCP biomaterial in anterior spine fusion. Both beta-TCP and beta-TCP+PRP had poorer radiological and histological outcomes than that of autograft after 3 months.

L23 ANSWER 4 OF 43 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 1040083605 JICST-EPlus
TITLE: Surgical treatment of bone defects with novel interconnected **porous hydroxyapatites ceramics**
AUTHOR: TAMAI NOBUYUKI; MYOI AKIRA; KAITO TAKASHI; MURASE TSUYOSHI; UEDA TAKAFUMI; OCHI TAKAHIRO
ARAKI NOBUHITO
AKITA SHOSUKE
NAKASE TAKAMASA
CORPORATE SOURCE: Graduate School of Medicine, Osaka Univ., JPN
Osaka Medical Center for Cancer and Cardiovascular Diseases, Hospital, JPN
Social Insurance, Hoshigaoka Koseinenkin Hospital, JPN
Kokuritsubyoin'osakairyose Seikeigeka
SOURCE: Kansetsu Geka (Journal of Joint Surgery), (2004) vol. 23, no. 2, pp. 256-263. Journal Code: S0169B (Fig. 6, Ref. 14)
ISSN: 0286-5394
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Commentary
LANGUAGE: Japanese
STATUS: New
AB **Hydroxyapatite** (HA) is useful as an artificial bone with biocompatibility. Features of novel interconnected HA **porous** NEOBONE are described in order to solve problems by **porous** HA **ceramics.** Good clinical results are introduced. Clinical trials using NEOBONE are performed in 65 cases. Subjects are fractures, bone defects due to bone tumor, rheumatiod arthritis and osteoarthritis. Bone union is confirmed in the roentgenogram. 2 cases of adults are presented. In the basic research of NEOBONE, there are researches on the reinforcement of osteogenesis using vascular endothelial **growth factor** (VEGF). By adding NEOBONE and **BMP** (**bone morphogenetic** protein), ectopic bone formation in the porus **ceramics** is evaluated. Clinical application of a 19-year-old woman with malignant bone tumor is introduced, which used NEOBONE jointly for the own bone transplantation as a **method** for filling enormous bone defect.

L23 ANSWER 5 OF 43 JICST-EPlus COPYRIGHT 2005 JST on STN

ACCESSION NUMBER: 1040714340 JICST-EPlus
TITLE: Artificial **Bone Grafts** NEOBONE
AUTHOR: IMURA KOICHI
CORPORATE SOURCE: Toshiba Ceramics Co., Ltd.
SOURCE: Nippon Kessho Seicho Gakkaishi (Journal of the Japanese Association of Crystal Growth), (2004) vol. 31, no. 2, pp. 73-77. Journal Code: F0452B (Fig. 8, Ref. 8)
ISSN: 0385-6275
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB Artificial **bone grafts**: NEOBONE are consists of **porous sintered** body which made of **hydroxyapatite ceramics**, it has unique pore structure. The NEOBONE with about 75% porosity and 150-200 Mm of mean pore diameter is connected entirely through interconnected pore which diameter is more than 10 Mm. The struts of **porous** body are fine **sintered.** Despite it has high porosity, the compressive strength is about 15 MPa which has relatively high mechanical strength. In pre-clinical test, living tissue could penetrate rapidly in the central part of the NEOBONE. At the 6 weeks after implantation, matured myeloid tissue had formed. This is attributed to pore structure of NEOBONE, and in this point, it is different from other artificial **bone grafts.** NEOBONE is already got a manufacturing approval from Ministry of Health, Labor and Welfare, and now start to production and distribution for clinical use. In the future, this artificial **bone grafts** may be used in regenerative medical **technique** and tissue engineering field. (author abst.)

L23 ANSWER 6 OF 43 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 1030662953 JICST-EPlus
TITLE: Bone regeneration therapy by marrow mesenchymal cells
AUTHOR: YOSHIKAWA TAKAAKI
CORPORATE SOURCE: Nara Med. Univ.
SOURCE: Kansetsu Geka (Journal of Joint Surgery), (2003) vol. 22, no. 10, pp. 1266-1274. Journal Code: S0169B (Fig. 9, Ref. 19)
ISSN: 0286-5394
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Commentary
LANGUAGE: Japanese
STATUS: New
AB Regeneration of tissues, especially bone and dermis, by bone marrow mesenchymal cells is explained. Culture **method** produced efficiently liquid of the marrow mesenchymal cells is described. There are various problems in the transplantation of own bone, artificial bone and homogeneous bone. **Method** is devised that cultured and multiplicated marrow mesenchymal cells in **porous** high **ceramics** are mixed and transplants. It is more sufficient if a little **BMP** is adsorbed. **Method** is described that marrow mesenchymal cells are as carrier contained in a collagen sponge for the fracture healing. **Method** built the marrow mesenchymal cells in a **porous** artificial head is described. Artificial dermis is introduced for skin injuries such as burn injury, bedsore and external wounds. **Porous ceramic**, collagen sponge and artificial joint graft are outlined on the osteogenesis by activated culture **bone graft.**

L23 ANSWER 7 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on

STN
ACCESSION NUMBER: 2003:352898 BIOSIS
DOCUMENT NUMBER: PREV200300352898
TITLE: Modification of gene expression induced in human osteogenic and osteosarcoma cells by culture on a biphasic **calcium phosphate** bone substitute.
AUTHOR(S): Rochet, N. [Reprint Author]; Loubat, A.; Laugier, J.-P.; Hofman, P.; Bouler, J. M.; Daculsi, G.; Carle, G. F.; Rossi, B.
CORPORATE SOURCE: Faculte de Medecine, UMR 6549 CNRS/UNSA, IFR50, Avenue de Valombrose, 06107, Nice Cedex 02, France rochet@unice.fr
SOURCE: Bone (New York), (June 2003) Vol. 32, No. 6, pp. 602-610. print.
CODEN: BONEDL. ISSN: 8756-3282.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jul 2003
Last Updated on STN: 30 Jul 2003

AB Bone hybrids made of **bioceramics** seeded with mesenchymal or osteoblastic cells are very promising alternatives to autologous **bone graft.** Along this line, the development of in vitro models, dedicated to analyze the influence of these biomaterials on osteogenic cells, will help to improve the performance of these bone substitutes. In the present work we analyzed the effects of a **macroporous** biphasic **calcium phosphate** **ceramic** (BCP, Triosite) on three different human osteosarcoma cell lines and on human primary osteogenic cells and compared this culture substratum to traditional culture on plastic. We showed that all these osteoblastic cells adhere and proliferate on the trabecular BCP blocks, with a different spatial organization for osteosarcoma cells compared to normal osteogenic cells. We also demonstrated that osteoblastic marker genes such as Cbfa1, type I collagen, osteonectin, osteopontin, and osteocalcin were expressed at similar levels by these cells cultured on either substratum, suggesting that adhesion to BCP does maintain the osteoblastic phenotype of these cells. Next, we provided the first evidence of differences of cytokine expression profiles revealed on this Ca-P **ceramic** as compared to expression in classical culture. These modifications affected the expression of cytokines such as TGF-beta1, G-CSF, and IL-3 and were quantitatively different between osteosarcoma cells and normal osteogenic cells. Given the role of these cytokines in bone biology and in hematopoiesis, these results obtained in vitro suggest that the BCP **ceramic** studied here could stimulate osteogenesis in vivo by activating cellular processes during bone formation and healing. This study highlights the notion that the nature of the culture substratum must be taken into account when studying bone cell biology in vitro. Owing to the nature and spatial organization of the BCP, our hypothesis is that culture on BCP is closer to the physiological situation than culture on plastic.

L23 ANSWER 8 OF 43 MEDLINE on STN
ACCESSION NUMBER: 2003465158 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14526441
TITLE: Anterior lumbar intervertebral fusion with artificial bone in place of autologous bone.
AUTHOR: Xu Weiguo; Chen Anmin; Feng Xu; Yin Weifeng
CORPORATE SOURCE: Department of Orthopedics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030.
SOURCE: Journal of Huazhong University of Science and Technology.

Medical sciences = Hua zhong ke ji da xue xue bao. Yi xue Ying De wen ban = Huazhong keji daxue xuebao. Yixue Yingdewen ban, (2003) 23 (3) 300-1.
Journal code: 101169627. ISSN: 1672-0733.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20031008
Last Updated on STN: 20031218
Entered Medline: 20031126

AB The feasibility of anterior lumbar intervertebral fusion with artificial bone in place of autogenous bone was investigated. **Porous hydroxyapatite** (HA)/ZrO2 **ceramics** loading **bone morphogenetic** protein (**BMP**) were implanted after removal of lumbar vertebral disc in rabbits. The adjacent intervertebral discs were also removed by the same way and autogenous illic bone was implanted. SEM observation and biomechanical test were carried out. Compound bone had a bit lower **osteoinductive** activity than autogenous bone by SEM (**Osteoinductive** activity of artificial bone in 12 weeks was the same as that of autogenous bone in 9 weeks). Biomechanical test revealed that compound bone had lower anti-pull strength than autogenous bone ($P < 0.001$), but there was no significant difference in anti-pull strength between compound bone at 12th week and autogenous bone at 9th week ($P > 0.05$). It was concluded that compound bone could be applied for anterior spinal fusion, especially for those patients who can't use autogenous bone.

L23 ANSWER 9 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003347224 EMBASE
TITLE: [Hard tissue-implant interactions-2: Bone-**ceramic** and bone-polymer interactions].
SERT DOKU-BIYOMATERYAL ETKILESIMLERI-2: KEMIK-SERAMIK VE KEMIK-POLIMER ETKILESIMLERI.
AUTHOR: Korkusuz F.; Senkoylu A.; Korkusuz P.
CORPORATE SOURCE: F. Korkusuz, Orta Dogu Teknik Universitesi, Saglik ve Rehberlik Merkezi, 06531 Ankara, Turkey
SOURCE: Artroplasti Artroskopik Cerrahi, (2003) 14/2 (109-125).
Refs: 137
ISSN: 1300-0594 CODEN: AACEFT
COUNTRY: Turkey
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 009 Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
LANGUAGE: Turkish
SUMMARY LANGUAGE: English; Turkish

AB **Ceramics** commonly used in orthopedic surgery and traumatology as bone substitutes are of **hydroxyapatite** (HA), **tricalcium phosphate** (TCP) and **glass** origin. The advantage of **ceramics** over metals is their biological interaction with the implanted host tissue. **Ceramics** were so far described as biocompatible and biologically active materials. Recent studies, however, indicate that when implanted into the bone marrow, these implants can induce non-specific bone marrow **inflammation** and cellular depletion. **Glass** inomers are recently used to improve **ceramics** mechanical strength. These inomers, on the other hand,

may cause adverse effects on neural tissues. Tissue necrosing heat of bone cement without changing its mechanical properties is trying to be reduced in recent years. Adding HA into the bone cement (PMMA) is a **method** that can be used for this reason. The biocompatibility of bone cement can also be improved by this **method.** Polymerization heat of bone cement can be decreased from 111°C to 87°C by adding HA into PMMA. This also increased the compressive strength of the bone cement. Injectable **calcium phosphate** cement is also a novel development in the field of bone **ceramics.** Polimers are mainly used for fracture fixation, bone replacement, cartilage regeneration, ligament and tendon fixation and controlled release of medicine. Following their clinical application, sterile sinus drainage and osteolysis around the implants are signs of tissue response. As the size of these implants increase the tissue reaction towards the implant is suspectected to increase. Hard tissue engineering will rise on the shoulders of appropriate **scaffolds**, local mediators and osteogenic cells in the near future. Tissue engineers should seek for **scaffolds** as close as to the bones elastic and rigid properties. **Bioceramics** are materials that mimic the mineral phase of the bone being good candidates as appropriate **scaffolds.**

L23 ANSWER 10 OF 43 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002101830 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11818845
TITLE: A 1-year study of osteoinduction in **hydroxyapatite** -derived biomaterials in an adult sheep model: part I.
AUTHOR: Gosain Arun K; Song Liansheng; Riordan Paul; Amarante Marco T; Nagy Paul G; Wilson Charles R; Toth Jeffrey M; Ricci John L
CORPORATE SOURCE: Department of Plastic Surgery, Medical College of Wisconsin, Milwaukee, 53226, USA.. akgosain@mcw.edu
SOURCE: Plastic and reconstructive surgery, (2002 Feb) 109 (2) 619-30.
Journal code: 1306050. ISSN: 0032-1052.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020209
Last Updated on STN: 20020222
Entered Medline: 20020221

AB The study presented here investigated **hydroxyapatite** biomaterials implanted in soft-tissue sites in adult sheep to determine whether these materials are **osteoinductive** and whether the rate of osteoinduction can be increased by manipulating the composition and porosity of the implants. For the study, 16.8-mm x 5-mm discs were prepared from mixtures of **hydroxyapatite** and beta-**tricalcium phosphate.** Five mixtures of **hydroxyapatite-ceramic** and **hydroxyapatite** -cement paste forms were studied: 100 percent **hydroxyapatite-ceramic** (Interpore), 60 percent **hydroxyapatite-ceramic**, 100 percent **hydroxyapatite**-cement paste, 60 percent **hydroxyapatite**-cement paste, and 20 percent **hydroxyapatite**-cement paste. Biomaterials were implanted in subcutaneous and intramuscular soft-tissue pockets in 10 adult sheep. Cranial **bone grafts** of equal dimension were implanted as controls. One year after implantation, the volume of all biomaterials and **bone grafts** was determined from a computed tomographic scan, and porosity and bone formation were determined using

backscatter electron microscopy. Cranial bone and the 20 percent **hydroxyapatite**-cement paste implants demonstrated significant volume reduction in all sites after 1 year ($p < 0.001$). No significant difference in volume of the remaining four biomaterials was found. There was no significant change in pore size in the **ceramic** implants (range, 200 to 300 micro) and in the cement-paste implants containing 60 percent **hydroxyapatite** or more (range, 3 to 5 nm). Pore size in the cement-paste implants containing 20 percent **hydroxyapatite** increased significantly with resorption of the **tricalcium-phosphate** component, reaching a maximum of 200 to 300 micro in the periphery, where the greatest **tricalcium-phosphate** resorption had occurred. Both **ceramic** biomaterials demonstrated lamellar bone deposition within well-formed haversian systems through the entire depth of the implants, ranging from a mean of 6.6 percent to 11.7 percent. There was minimal bone formation in the cement-paste implants containing 60 percent **hydroxyapatite** or more. In contrast, cement-paste implants containing 20 percent **hydroxyapatite** demonstrated up to 10 percent bone replacement, which was greatest in the periphery of the implants where the greatest **tricalcium-phosphate** resorption had occurred. This study confirms the occurrence of true osteoinduction within **hydroxyapatite**-derived biomaterials, when examined using backscatter **techniques.** In this study, the rate of osteoinduction was greatest when a **porous** architecture was maintained, which was best achieved in **ceramic** rather than cement-paste forms of **hydroxyapatite.** Porosity and resultant bone formation in cement-paste implants can be improved by combining **hydroxyapatite** with a rapidly resorbing component, such as **tricalcium phosphate.**

L23 ANSWER 11 OF 43 MEDLINE on STN
ACCESSION NUMBER: 2002298417 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12038849
TITLE: Applications of **calcium phosphate**-based cancellous bone void fillers in trauma surgery.
AUTHOR: Szpalski Marek; Gunzburg Robert
CORPORATE SOURCE: Department of Orthopedic Surgery, Centre Hospitalier Moliere Longchamp, Brussels, Belgium.
SOURCE: Orthopedics, (2002 May) 25 (5 Suppl) s601-9. Ref: 62
Journal code: 7806107. ISSN: 0147-7447.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020602
Last Updated on STN: 20021211
Entered Medline: 20021115

AB For more than a century, fracture repair has been augmented with autogenous cancellous **bone grafting**, which supplies 3 requisite properties: **growth factors** for osteoinduction, progenitor stem cells for osteogenesis, and **scaffolding** for osteoconduction. However, disadvantages to using autogenous bone include procurement morbidity, longer operative time, and limited availability. Allograft is more readily available but does not supply **osteoinductive** or osteogenic properties. Better alternatives for **bone grafting** currently include autologous bone marrow, **ceramics**, allograft demineralized bone matrix, and regulatory **growth factors**; however, none

of these fulfills all 3 requisite properties. Replacement or augmentation of autograft with a **calcium phosphate**-based composite graft, which combines the best elements of each component into a single engineered graft, is discussed.

L23 ANSWER 12 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003146050 EMBASE
TITLE: Limitations of autograft and allograft: New synthetic solutions.
AUTHOR: Betz R.R.
CORPORATE SOURCE: Dr. R.R. Betz, Shriners Hospital for Children, Philadelphia, PA, United States
SOURCE: Orthopedics, (1 May 2002) 25/5 SUPPL. (s561-s570). Refs: 86
ISSN: 0147-7447 CODEN: ORTHDK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Autogenous cancellous bone is widely regarded as an ideal construct for graft procedures, supplying **osteoinductive growth factors**, osteogenic cells, and a structural **scaffold.** However, procurement morbidity and constraints on obtainable quantities limit its use. Allograft is the next best alternative at present; however, minor immunologenic rejection and risk of disease transmission are unresolved issues. Although synthetic grafting materials eliminate these risks, these materials do not transfer **osteoinductive** or osteogenic elements to the host site. To offer the advantages of autograft and allograft, a composite graft may be considered. Such a graft can combine a synthetic **scaffold** with biologic elements to stimulate cell infiltration and new bone formation.

L23 ANSWER 13 OF 43 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2002158961 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11880831
TITLE: How does recombinant human **bone morphogenetic** protein-4 enhance posterior spinal fusion?.
AUTHOR: Cheng Jack C Y; Guo Xia; Law Lai Pang; Lee Kwong Man; Chow Daniel H K; Rosier Randy
CORPORATE SOURCE: Department of Orthopaedics, The Chinese University of Hong Kong, the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong.. jackcheng@cuhk.edu.hk
SOURCE: Spine, (2002 Mar 1) 27 (5) 467-74. Journal code: 7610646. ISSN: 1528-1159.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020314
Last Updated on STN: 20020528
Entered Medline: 20020522

AB STUDY DESIGN: A rabbit posterolateral intertransverse process fusion model was used to evaluate the effect that different doses of recombinant human

bone morphogenetic protein-4 delivered in a **porous hydroxyapatite-tricalcium phosphate ceramic** had on osteogenesis and spinal fusion. OBJECTIVE: To study the biologic effect and threshold dose of recombinant human **bone morphogenetic** protein-4 in enhancing spinal fusion. SUMMARY OF BACKGROUND DATA: Biologic manipulation for spinal fusion is an area undergoing active research. The enhancing effects of recombinant human **bone morphogenetic** proteins 2 and 7 on spinal fusion have been proved, and clinical trials of their application are in progress. Recombinant human **bone morphogenetic** protein-4 is another **osteoinductive** protein that has the ability to induce heterotopic bone formation, and its potential for enhancing spinal fusion has not yet been studied. **METHODS**: For this study, 24 adult New Zealand white rabbits underwent single-level unilateral posterior intertransverse process spinal fusion at L5-L6. The animals were divided into four groups using different graft materials: allograft as well as **hydroxyapatite-tricalcium phosphate** augmented with 0, 1.25, and 5 microgram of recombinant human **bone morphogenetic** protein-4, respectively. The local changes were evaluated by sequential radiograph, manual palpation, histomorphology, and microradiography. RESULTS: At week 7, ossification in the intertransverse process area ceased in groups without recombinant human **bone morphogenetic** protein-4, whereas active multicentric endochondral bone formation was demonstrated in groups with this **growth factor.** The success rate of contiguous bony bridging was found to correlate positively with the dose of recombinant human **bone morphogenetic** protein-4. CONCLUSIONS: Recombinant human **bone morphogenetic** protein-4 effectively enhances new bone formation and accelerates fusion in the rabbit posterolateral posterior spinal fusion model. The effective dose of recombinant human **bone morphogenetic** protein-4 is 10 times lower than the reported dosage of recombinant human **bone morphogenetic** proteins 2 and 7.

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ACCESSION NUMBER: 2002:392762 BIOSIS
DOCUMENT NUMBER: PREV200200392762
TITLE: Histological characterization of the early stages of **bone morphogenetic** protein-induced osteogenesis.
AUTHOR(S): Vehof, J. W. M.; Takita, H.; Kuboki, Y.; Spauwen, P. H. M.; Jansen, J. A. [Reprint author]
CORPORATE SOURCE: Department of Biomaterials, College of Dental Science, University Medical Center Nijmegen, 6500 HB, P. O. Box 9101, Nijmegen, Netherlands
j.jansen@dent.kun.nl
SOURCE: Journal of Biomedical Materials Research, (September 5, 2002) Vol. 61, No. 3, pp. 440-449. print.
CODEN: JBMRBG. ISSN: 0021-9304.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2002
Last Updated on STN: 17 Jul 2002

AB On the basis of currently available knowledge, we hypothesize that the initial bone formation, as induced by **bone morphogenetic** protein (**BMP**), is influenced by the chemical composition and three-dimensional spatial configuration of the used carrier material. Therefore, in the current study, the **osteoinductive** properties

of **porous** titanium (Ti) fiber mesh with a **calcium phosphate** (Ca-P) coating (Ti-CaP), insoluble bone matrix (IBM), fibrous **glass** membrane (FGM), and **porous** particles of **hydroxy apatite** (PPHAP) loaded with rhBMP-2 were compared in a rat ectopic assay model at short implantation periods. Twelve Ti-CaP, 12 IBM, 12 FGM, and 12 PPHAP implants, loaded with rhBMP-2, were subcutaneously placed in 16 Wistar King rats. The rats were sacrificed at 3, 5, 7, and 9 days post-operative, and the implants were retrieved. Histological analysis demonstrated that IBM and Ti-CaP had induced ectopic cartilage and bone formation by 5 and 7 days, respectively. However, in PPHAP, bone formation and cartilage formation were seen together at 7 days. At 9 days, in Ti-CaP, IBM, and PPHAP, cartilage was seen together with trabecular bone. At 9 days, in FGM, only cartilage was observed. Quantitative rating of the tissue response, using a scoring system, demonstrated that the observed differences were statistically significant (Wilcoxon rank sum test, $p<0.05$). We conclude that IBM, CaP-coated Ti mesh, FGM, and PPHAP provided with rhBMP-2 can indeed induce ectopic bone formation with a cartilaginous phase in a rat model at short implantation periods. Considering the different chemical composition and three-dimensional spatial configuration of the carrier materials used, these findings even suggest that endochondral ossification is present in rhBMP-2-induced osteogenesis, even though the amount of cartilage may differ.

L23 ANSWER 15 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:117921 BIOSIS
DOCUMENT NUMBER: PREV200200117921
TITLE: Adsorption and release properties of **growth factors** from biodegradable implants.
AUTHOR(S): Ziegler, J.; Mayr-Wohlfart, U. [Reprint author]; Kessler, S.; Breitig, D.; Guenther, K.-P.
CORPORATE SOURCE: Orthopaedic Department (RKU), University of Ulm, Oberer Eselsberg 45, 89081, Ulm, Germany
uschi.mayrwohlfart@medizin.uni-ulm.de
SOURCE: Journal of Biomedical Materials Research, (March 5, 2002) Vol. 59, No. 3, pp. 422-428. print.
CODEN: JBMRBG. ISSN: 0021-9304.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2002
Last Updated on STN: 21 Mar 2002

AB The present investigation was performed to study the adsorption behavior of **growth factors** and their release characteristics from biodegradable implants in an in vitro study. We investigated the stability of **growth factors** administered on various **scaffolds**. We used **porous tricalcium phosphate ceramics** (alpha-TCP), a neutralized **glass-ceramics** (GB9N), a composite (polylactid/-glycolid/GB9N), and solvent dehydrated human bone as carriers. Block shaped **scaffolds** (sized: 7 X 7 X 10 mm) were loaded with 5 mug of either **bone morphogenetic** protein (rxBMP-4), basic fibroblast **growth factor** (rh-bFGF), or vascular endothelial **growth factor** (rh-VEGF) solved in 150 muL PBS. The **growth factors** were labeled with Iodine125 (I-125) for detecting the adsorbed and released amount of **growth factors** by counting the samples for total I-125 activity. We observed that the adsorption of these **growth factors** seems to depend on two different parameters: first on the nature of the tested material, and second on the **growth factors** on

their own. The release kinetics of the **growth factors** from the biodegradable implants can be described as a two phase process-a very rapid release during the first hours by an elution of not adsorbed protein, followed by a specific release, which depends upon the chemical/physical interaction of the material and the **growth factor** used. Analyzing the eluted proteins on SDS-PAGEs rh-VEGF was degraded into a smaller fragment with a size of around 15 kDa, while rxBMP-4 and rh-bFGF showed a complete degradation into fragments smaller than 3 kDa after more than 3 days. Although this in vitro study suggests that biodegradable implants might be successfully used as carriers for osteogenic **growth factors**, the different release kinetics as well as the alteration of their molecular structure including loss of biological activity should be considered.

L23 ANSWER 16 OF 43 MEDLINE on STN
ACCESSION NUMBER: 2002159498 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11890685
TITLE: **Adenoviral BMP**-2 gene transfer in mesenchymal stem cells: in vitro and in vivo bone formation on biodegradable polymer **scaffolds.**
AUTHOR: Partridge Kris; Yang Xuebin; Clarke Nicholas M P; Okubo Yasunori; Bessho Kazuhisa; Sebald Walter; Howdle Steven M; Shakesheff Kevin M; Oreffo Richard O C
CORPORATE SOURCE: University Orthopaedics, University of Southampton, General Hospital, Southampton SO16 6YD, United Kingdom.
SOURCE: Biochemical and biophysical research communications, (2002 Mar 22) 292 (1) 144-52.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020314
Last Updated on STN: 20020501
Entered Medline: 20020430

AB The aim of this study was to determine the feasibility of **adenoviral** gene transfer into primary human bone marrow osteoprogenitor cells in combination with biodegradeable **scaffolds** to tissue-engineer bone. Osteoprogenitors were infected with AxCAOBMP-2, a vector carrying the human **BMP**-2 gene. Alkaline phosphatase activity was induced in C2C12 cells following culture with conditioned media from **BMP**-2 expressing cells, confirming successful secretion of active **BMP**-2. Expression of alkaline phosphatase activity, type I collagen and mineralisation confirmed bone cell differentiation and maintenance of the osteoblast phenotype in extended culture for up to 6 weeks on PLGA **porous scaffolds.** In vivo implantation of **adenoviral** osteoprogenitor constructs on PLGA biodegradeable **scaffolds**, using diffusion chambers, also demonstrated bone cell differentiation and production of bone tissue. The maintenance of the osteoblast phenotype in extended culture and generation of mineralised 3-D **scaffolds** containing such constructs indicate the potential of such bone tissue engineering approaches in bone repair. (C)2002 Elsevier Science (USA).

L23 ANSWER 17 OF 43 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 1020547958 JICST-EPlus
TITLE: Experimental studies on bone induction using low-molecular-weight poly (DL-lactide-co-glycolide) as a carrier for recombinant human **bone**

morphogenetic protein-2.
AUTHOR: BESSHO K
CARNES D L; CAVIN R; ONG J L
CORPORATE SOURCE: Kyoto Univ., Kyoto, Jpn
Univ. Texas Health Sci. Center At San Antonio, Texas
SOURCE: J Biomed Mater Res, (2002) vol. 61, no. 1, pp. 61-65.
Journal Code: E0528A (Fig. 6, Ref. 14)
CODEN: JBMRBG; ISSN: 0021-9304
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New

L23 ANSWER 18 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:319066 BIOSIS
DOCUMENT NUMBER: PREV200100319066
TITLE: Poly(lactide-co-glycolide)/**hydroxyapatite** delivery of **BMP**-2-producing cells: A regional gene therapy approach to bone regeneration.
AUTHOR(S): Laurencin, C. T. [Reprint author]; Attawia, M. A.; Lu, L. Q.; Borden, M. D.; Lu, H. H.; Gorum, W. J.; Lieberman, J. R.
CORPORATE SOURCE: Department of Chemical Engineering, Center for Advanced Biomaterials and Tissue Engineering, Drexel University, 3141 Chestnut Street, Philadelphia, PA, 19104, USA
laurencin@drexel.edu
SOURCE: Biomaterials, (June, 2001) Vol. 22, No. 11, pp. 1271-1277. print.
CODEN: BIMADU. ISSN: 0142-9612.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002
AB Currently, functional treatment of fracture non-unions and bone loss remains a significant challenge in the field of orthopaedic surgery. Tissue engineering of bone has emerged as a new treatment alternative in bone repair and regeneration. Our approach is to combine a polymeric matrix with a cellular vehicle for delivery of **bone morphogenetic** protein-2 (**BMP**-2), constructed through **retroviral** gene transfer. The objective of this study is to develop an **osteoinductive**, tissue-engineered bone replacement system by culturing **BMP**-2-producing cells on an osteoconductive, biodegradable, polymeric-**ceramic** matrix. The hypothesis is that **retroviral** gene transfer can be used effectively in combination with a biodegradable matrix to promote bone formation. First, we examined the in vitro attachment and growth of transfected **BMP**-producing cells on a PLAGA-HA **scaffold.** Second, the bioactivity of the produced **BMP** in vitro was evaluated using a mouse model. It was found that the polymer-**ceramic scaffold** supported **BMP**-2 production, allowing the attachment and growth of **retroviral** transfected, **BMP**-2-producing cells. In vivo, the **scaffold** successfully functioned as a delivery vehicle for bioactive **BMP**-2, as it induced heterotopic bone formation in a SCID mouse model.

L23 ANSWER 19 OF 43 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001314497 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11317116
TITLE: Evaluation of carriers of **bone**

morphogenetic protein for spinal fusion.
COMMENT: Comment in: Spine. 2001 Apr 15;26(8):850. PubMed ID: 11317102
AUTHOR: Minamide A; Kawakami M; Hashizume H; Sakata R; Tamaki T
CORPORATE SOURCE: Department of Orthopaedic Surgery, Wakayama Medical College, Wakayama City, Wakayama, Japan.. minamide@wakayama-med.ac.jp
SOURCE: Spine, (2001 Apr 15) 26 (8) 933-9.
Journal code: 7610646. ISSN: 0362-2436.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB STUDY DESIGN: Posterolateral lumbar transverse process fusion in a rabbit model was performed using two different carriers for recombinant human morphogenetic protein-2, one having a **porous** structure and the other being a Type I collagen sheet. OBJECTIVES: To compare the effectiveness of two different carriers for recombinant human morphogenetic protein-2 in achieving lumbar intertransverse process arthrodesis. SUMMARY OF BACKGROUND DATA: The application of **osteoinductive growth factors** at various anatomic sites, such as in long bones and spinal segments, has been performed experimentally by many researchers. Although many carriers of **osteoinductive** factors have been reported, the most effective carrier has not been established. We have reported the efficacy of **sintered** bovine bone, True Bone **Ceramics**, which is coated with Type I collagen as a carrier of recombinant human **bone morphogenetic** protein-2 in achieving lumbar intertransverse process arthrodesis. True Bone **Ceramics** is a crystallized form of bone minerals made from **sintering** bovine bone at high temperatures and possesses natural trabecular structure. The crystalline character of True Bone **Ceramics** is similar to that of artificial **hydroxyapatite.** In this study we focused on the structure of two different carriers to facilitate osteosynthesis in lumbar arthrodesis. **METHODS**: Fifty-four adult rabbits underwent bilateral lumbar intertransverse process arthrodesis at L4-L5. The animals were divided into five groups and had implants placed as follows: Group 1, autograft group, harvested autologous corticocancellous bone from the posterior iliac crest; Group 2, TBC group, True Bone **Ceramics** alone; Group 3, TBC-TBMP group, True Bone **Ceramics** coated with Type I collagen infiltrated with 100 microg of recombinant human **bone morphogenetic** protein-2; Group 4, collagen group, Type I collagen sheet; and Group 5, collagen-**BMP** group, implanted collagen sheet containing 100 microg of recombinant human **bone morphogenetic** protein-2. Spinal fusion was evaluated by radiographic analysis, manual palpation, biomechanical testing, and histologic examination at both 3 and 6 weeks after surgery. RESULTS: Radiographs in the TBC-TBMP group showed a continuous trabecular pattern within the intertransverse area at 3 weeks after surgery. The fusion mass in the intertransverse area was more prominent than in the other groups. At 3 weeks after surgery the TBC-TBMP group had higher fusion rates based on manual palpation, and the fusions showed significantly higher tensile strength and stiffness. The histologic findings in the TBC-TBMP group at 3 weeks after surgery showed a cortical bone rim around the edge of the fusion mass, and contiguous new bone appearing between the recipient bone and the matrix of TBC without evidence of foreign body formation. In the

collagen-**BMP** group, less mature bone formation was present within the grafted area and the new bone was not contiguous, even at 6 weeks after surgery. CONCLUSIONS: As a carrier for recombinant human **bone morphogenetic** protein-2, True Bone **Ceramics**, possessing a bony or **porous** structure, was more effective than a Type I collagen sheet in achieving a faster and stronger lumbar spinal fusion in a rabbit model.

L23 ANSWER 20 OF 43 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001669947 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11716010
TITLE: **Porous tricalcium phosphate** and transforming **growth factor** used for anterior spine surgery.
AUTHOR: Steffen T; Stoll T; Arvinte T; Schenk R K
CORPORATE SOURCE: Royal Victoria Hospital, Division of Orthopaedic Surgery, McGill University, Montreal, QC, Canada.. tsteffen@orl.mcgill.ca
SOURCE: European spine journal : official publication of the European Spine Society, European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society, (2001 Oct) 10 Suppl 2 S132-40. Journal code: 9301980. ISSN: 0940-6719.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20011122
Last Updated on STN: 20020404
Entered Medline: 20020402

AB Harvesting autologous **bone graft** from the iliac crest is associated with considerable secondary morbidity. **Bone graft** substitutes such as **porous ceramics** are increasingly used for spinal surgery. This paper presents the results of an animal study in which beta-**tricalcium phosphate** (beta-TCP) bone substitutes were used for anterior spinal surgery in sheep and baboons. The presented baboon study also investigated the effect of impregnating the **ceramic** material with transforming **growth factor** (TGF). In the first study, using the sheep model, a stand-alone instrumented anterior fusion was performed. The animals were randomized into three treatment groups: autologous bone, beta-TCP granules, and sham group. The results were analyzed biomechanically and histologically at three survival intervals: 8, 16 and 32 weeks. An additional animal group was added later, with **ceramic** pre-filled implants. In the second study, a baboon model was used to assess the osteointegration of a 15-mm-diameter **porous** beta-TCP block into the vertebral body. The experiment was partially motivated by a new surgical procedure proposed for local **bone graft** harvest. Three treatment groups were used: beta-TCP plug, beta-TCP plug impregnated with TGF-beta3, and a sham group with empty defect. The evaluation for all animals included computer tomograms at 3 and 6 months, as well as histology at 6 months. In the sheep model, the mechanical evaluation failed to demonstrate differences between treatment groups. This was because massive anterior bone bridges formed in almost all the animals, masking the effects of individual treatments. Histologically, beta-TCP was shown to be a good osteoconductor. While multiple signs of implant micromotion were documented, pre-filling the cages markedly improved the histological fusion outcomes. In the baboon study, the beta-TCP plugs were completely osteointegrated at 6 months.

For the group that used **ceramic** plugs impregnated with TGF-beta3, no incremental advantage was seen as a result of this particular application. However, TGF-beta3 is a potent **growth factor** at a very low dose. Not only does it speed up the **ceramic** material resorption, but it is also responsible for massive regional new bone formation. More experiments are required to better understand the biological effects of this **growth factor** in relation to bone formation, and to be able to take clinical advantage of them.

L23 ANSWER 21 OF 43 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001245828 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11240533
TITLE: [In vitro assessment of combining osteogenic cells with **macroporous calcium-phosphate ceramics**].
Etude in vitro de l'association de cellules osteogenes avec une ceramique en phosphate de calcium macroporeuse.
AUTHOR: Heymann D; Delecrin J; Deschamps C; Gouin F; Padrines M; Passuti N
CORPORATE SOURCE: EE 99-01, Laboratoire de Physiopathologie de la Resorption Osseuse, Nantes, France.. dominique.heymann@sante.univ-nantes.fr
SOURCE: Revue de chirurgie orthopedique et reparatrice de l'appareil moteur, (2001 Feb 1) 87 (1) 8-17.
Journal code: 1272427. ISSN: 0035-1040.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB PURPOSE OF THE STUDY: **Bone grafts** or bone substitutes are required to fill bone defects resulting from trauma or surgical resection of tumors. **Calcium-phosphate ceramics** are synthetic bone substitutes which promote new bone formation by osteoconduction. These **ceramics** possess osteoconductive properties but have no intrinsic **osteoinductive** capacity. They are unable to induce new bone formation in extraossesous sites. One solution to develop bone substitutes with osteogenic properties would be to associate biomaterials with osteoprogenitors. MATERIALS AND **METHODS**: We studied the in vitro osteogenic potential of human bone-marrow cells cultured on **macroporous calcium phosphate** (CaP) **ceramic**, examining stromal cell proliferation and differentiation. Osteogenic differentiation was evaluated in terms of alkaline phosphatase activity and immunological characterization of the extracellular fibrillar matrix formed by these cells. The specimens were examined by scanning and transmission electron microscopy. RESULTS: Human bone-marrow cells proliferated on CaP **ceramic.** The proliferating bone-marrow cells expressed an osteoblastic phenotype as shown by alkaline phosphatase activity and synthesis in **ceramic** pores of an extracellular matrix composed of fibronectin, osteocalcin and collagen I. In addition, numerous microcrystals of apatite precipitated on the fibrillar matrix, producing a mineralized fibrillar network within the **ceramic.** CONCLUSION: This study demonstrates that human bone-marrow cells cultured on **macroporous** CaP **ceramic** do not lose their osteoblastic phenotype even after 21 days of culture, and that they can

induce osteogenesis in a CaP **ceramic** in vitro. This type of new "hybrid material" appears promising for the future.

L23 ANSWER 22 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:288137 BIOSIS
DOCUMENT NUMBER: PREV200000288137
TITLE: The importance of drug delivery systems in tissue engineering.
AUTHOR(S): Tabata, Yasuhiko [Reprint author]
CORPORATE SOURCE: Institute for Frontier Medical Sciences, Kyoto University, 53 Kawara-cho Shogoin Sakyo-ku, Kyoto, 606-8507, Japan
SOURCE: Pharmaceutical Science and Technology Today, (March, 2000) Vol. 3, No. 3, pp. 80-89. print.
ISSN: 1461-5347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Jul 2000
Last Updated on STN: 7 Jan 2002
AB Tissue engineering is designed to regenerate natural tissues or to create biological substitutes for defective or lost tissues and organs through the use of cells. In addition to cells and their **scaffolds**, **growth factors** are required to promote tissue regeneration. Indeed, **growth factor**-induced vascularization is effective in supplying the oxygen and nutrients necessary for the survival of transplanted cells in organ substitution. However, **growth factors** have poor in vivo stability and so the biological effects are often unpredictable unless the delivery system is contrived. This review provides several examples to emphasize the importance of drug delivery systems in tissue engineering.

L23 ANSWER 23 OF 43 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1999444598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10515009
TITLE: Experimental spinal fusion using **sintered** bovine bone coated with type I collagen and recombinant human **bone morphogenetic** protein-2.
AUTHOR: Minamide A; Tamaki T; Kawakami M; Hashizume H; Yoshida M; Sakata R
CORPORATE SOURCE: Department of Orthopedic Surgery, Wakayama Medical College, Japan.. minamide@wakayama-med.ac.jp
SOURCE: Spine, (1999 Sep 15) 24 (18) 1863-70; discussion 1871-2.
Journal code: 7610646. ISSN: 0362-2436.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991028
AB STUDY DESIGN: Posterolateral lumbar transverse process fusion using recombinant human **bone morphogenetic** protein (rhBMP)-2 carried by **sintered** bovine bone and Type I collagen complex was compared with fusion achieved using autogeneous **bone graft** or **sintered** bovine bone alone. OBJECTIVES: This study examined the efficacy of **sintered** bovine bone coated with Type I collagen as a carrier of rhBMP-2 for lumbar intertransverse process arthrodesis. SUMMARY OF BACKGROUND DATA: Posterolateral intertransverse process arthrodesis using **osteoinductive growth**

factors is performed experimentally in the lumbar spine. The previous studies revealed the efficacy of **osteoinductive** factors applied to carriers having no bony structures, such as collagen sheet or polylactic acid polymer, for the spinal fusion. However, in their studies, a large amount of **osteoinductive** proteins have been applied for the spinal fusion. We used the **sintered** bovine bone "True Bone **Ceramics**" (TBC; Koken Co., Tokyo, Japan) coated with type I collagen as the carrier. True Bone **Ceramics** is the only biomaterial possessing a natural trabecular structure and an organized crystal of bone minerals. **METHODS**: Twenty-two adult rabbits underwent bilateral lumbar intertransverse process arthrodesis at L4-L5. The animals were divided into four groups and had materials implanted as follows: autologous bone group, grafted autologous corticocancellous bone harvested from the posterior iliac crest; implanted TBC group; TBC collagen group, implanted TBC coated with Type I collagen infiltrating into the **porous** space; and **BMP** group, implanted **sintered** bovine bone coated with Type I collagen infiltrated with 100 micrograms of rhBMP-2. Spinal fusion was evaluated by radiographic analysis, manual palpation, biomechanical testing, and histologic examination 6 weeks after surgery. RESULTS: Two rabbits were killed because of infection and lumbar plexus palsy. Radiographs of the **BMP** group showed a homogeneous fusion mass at the intertransverse area, and stability was confirmed by dynamic radiographs at 3 and 6 weeks after surgery. In the **BMP** group, a bony mass in the intertransverse area was more prominent than in the other groups. The **BMP** group had a higher fusion rate based on manual palpation than the-other groups, and **BMP** fusions showed significantly higher tensile strength and stiffer fusion. The histologic findings in the **BMP** group demonstrated membranous bone and endochondral bone formations between the transverse process and the fusion mass. In the other groups, continuous trabecular bone formation was observed in the area surrounding the transverse process, but gaps between grafted fragments and less mature bone formation were present in the intertransverse area. CONCLUSIONS: **Sintered** bovine bone coated with Type I collagen and rhBMP-2 resulted in a higher fusion rate than the autograft and can be used as a carrier for rhBMP-2 in spinal fusion.

L23 ANSWER 24 OF 43 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000190716 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10726511
TITLE: Biomaterials in the face: benefits and risks.
AUTHOR: Gosain A K; Persing J A
CORPORATE SOURCE: Department of Plastic Surgery, Medical College of Wisconsin, Milwaukee, WI 53226, USA.
SOURCE: Journal of craniofacial surgery, (1999 Sep) 10 (5) 404-14. Ref: 48
Journal code: 9010410. ISSN: 1049-2275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Conference; Conference Article; (CONGRESSES)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Space Life Sciences
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000328

AB An extensive review of biomaterials in the face was conducted in an American Society of Maxillo-facial Surgeons-sponsored biomaterials

symposium. The symposium was held in Boston, MA, immediately preceding the 1998 annual meeting of the ASPRS/PSEF. The scope of the symposium extended from current reconstructive **techniques** for the facial skeleton, including autogenous bone and biomaterials, to potential application of new **techniques** in molecular biology that may enable the body's own tissues to be engineered to provide bone and cartilage to reconstruct the facial skeleton. The authors review the presentations and relevant literature on biomaterials in the face. The following topics are reviewed: current reconstructive **techniques** using autogenous **bone grafts**, methyl methacrylate cranioplasty, demineralized bone, and **hydroxyapatite**; biomaterials used for rigid fixation, including metallic and bioabsorbable implants; biomaterials used for facial augmentation, including **porous** polyethylene, hard-tissue replacement, and **ceramic** biomaterials; biofilm, or a layered polysaccharide matrix secreted by **bacteria** on the surface of implants; and potential means of inducing bone formation by directing the body's own tissues through cytokine interaction, gene transfer, and tissue engineering.

L23 ANSWER 25 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2000:20758 BIOSIS
DOCUMENT NUMBER: PREV200000020758
TITLE: **Sintered porous hydroxyapatites** with intrinsic **osteoinductive** activity: Geometric induction of bone formation.
AUTHOR(S): Ripamonti, U. [Reprint author]; Crooks, J.; Kirkbride, A. N.
CORPORATE SOURCE: Bone Research Unit, Medical Research Council, University of the Witwatersrand Medical School, 7 York Road, Parktown, Johannesburg, 2193, South Africa
SOURCE: South African Journal of Science, (Aug., 1999) Vol. 95, No. 8, pp. 335-343. print.
CODEN: SAJSAR. ISSN: 0038-2353.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Dec 1999
Last Updated on STN: 31 Dec 2001

AB **Sintered hydroxyapatites** induce bone formation in adult baboons via intrinsic **osteoinductivity** regulated by the geometry of the substratum. Bone is thereby formed without exogenous **bone morphogenetic** proteins (BMPs), well-characterized inducers of bone formation. Monolithic discs of **sintered hydroxyapatite**, fabricated with concavities of 800 and 1600 mum diameter on both planar surfaces, were implanted in the rectus abdominis of the baboon (Papio ursinus). Histology on days 30 and 90 revealed de novo generation of bone exclusively within the concavities of the substratum. **Porous hydroxyapatites** were subsequently fabricated by impregnating polyurethane foams with slurry preparations of powdered **hydroxyapatite**, so that **porous** spaces formed by the coalescence of repetitive sequences of concavities. Artefacts were **sintered** in rod and disc configurations for implantation in heterotopic intramuscular sites and orthotopic calvarial sites, respectively. In four specimens, bone had formed in concavities of the substratum 30 days after implantation in the rectus abdominis. On day 90, **bone morphogenesis** with associated marrow had occurred in 33 specimens (41 %). Calvarial specimens showed substantial bone formation, culminating in complete penetration of bone within the **porous** spaces. On day 30, the immunolocalization of **BMP** family members (**BMP**-3 and OP-1/**BMP**-7) in cellular

material at the **hydroxyapatite** interface suggests that the **sintered ceramic** may act as a solid-state matrix for adsorption of endogenously produced BMPs. These experiments demonstrate intrinsic **osteoinductivity** by monolythic and **porous** **sintered hydroxyapatites** implanted in heterotopic sites of adult primates, and that the geometry of the substratum profoundly regulates the expression of the osteogenic phenotype. The incorporation of specific biological activities into biomaterials achieved by manipulating the geometry of the substratum, defined as geometric induction of bone formation, will help engineer morphometric responses for therapeutic osteogenesis in clinical contexts.

L23 ANSWER 26 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:215549 BIOSIS
DOCUMENT NUMBER: PREV199900215549
TITLE: Use of **porous hydroxyapatite** graft containing recombinant human **bone morphogenetic** protein-2 for cervical fusion in a caprine model.
AUTHOR(S): Takahashi, Toshiyuki; Tominaga, Teiji [Reprint author]; Watabe, Noriaki; Yokobori, A. Toshimitu, Jr.; Sasada, Hiroshi; Yoshimoto, Takashi
CORPORATE SOURCE: Department of Neurosurgery, Kohnan Hospital, 4-20-1 Nagamachi-minami, Taihaku-ku, Sendai, 982-8523, Japan
SOURCE: Journal of Neurosurgery, (April, 1999) Vol. 90, No. 4 SUPPL., pp. 224-230. print.
CODEN: JONSAC. ISSN: 0022-3085.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 May 1999
Last Updated on STN: 26 May 1999

AB Object. The efficacy of recombinant human **bone morphogenetic** protein-2 (rhBMP-2) for enhancing anterior cervical spine interbody fusion when added to a **porous** **hydroxyapatite** (HA) graft was investigated. **Methods.** Fourteen mature goats underwent three-level anterior discectomies after induction of endotracheal anesthesia. **Porous** HA grafts that contained 0, 5, and 50 mug of rhBMP-2 were placed concurrently with anterior cervical spine plates to achieve interbody fusion. The fusion rate, radiological findings, biomechanical stiffness, and histological appearance were evaluated in 42 spinal units immediately and again at 4 and 12 weeks after graft and plate placement. At 12 weeks postsurgery, manual testing showed a 100% fusion rate in the spines with HA grafts containing high-dose rhBMP-2; however, only a 50% fusion rate was shown in spines with grafts that contained no or low-dose rhBMP-2. On radiographic and histological studies the process of solid fusion was seen to be more advanced in relation to the use of larger amounts of rhBMP-2. Biomechanical testing demonstrated significantly higher stiffness values for grafts that contained high-dose rhBMP-2 than those without rhBMP-2 in flexion at 4 weeks, as well as in flexion, extension, and lateral bending tests at 12 weeks. Histological analysis demonstrated that rhBMP-2 increased the amount of bone apposition on the surface of the implants and promoted bone formation in the **porous** structure without increasing the penetration distance. Conclusions. Through osteogenesis at the fusion site, the addition of rhBMP-2 to a **porous** HA **ceramic** graft enhances the rate of anterior cervical fusion.

L23 ANSWER 27 OF 43 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1999385458 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10458276
TITLE: Evaluation of human recombinant **bone morphogenetic** protein-2-loaded **tricalcium phosphate** implants in rabbits' bone defects.
AUTHOR: Laffargue P; Hildebrand H F; Rtaimate M; Frayssinet P; Amoureux J P; Marchandise X
CORPORATE SOURCE: Laboratoire de Biophysique, Unite Programmee de Recherche et d'Enseignement Scientifique, Equipe d'Accueil (UPRES EA) 1049, Faculte de Medecine, Lille, France.
SOURCE: Bone, (1999 Aug) 25 (2 Suppl) 55S-58S.
Journal code: 8504048. ISSN: 8756-3282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990927

AB **Porous** beta-**tricalcium phosphate** (betaTCP) has osteoconductive properties. The adsorption of human recombinant **bone morphogenetic** protein-2 (rhBMP-2) onto TCP could realize an **osteoinductive** bone substitute. We evaluated it on an animal model using dual-energy X-ray absorptiometry (DEXA) and solid-state 31P nuclear magnetic resonance (NMR) spectroscopy. BetaTCP cylinders loaded with rhBMP-2 were implanted into rabbits' femoral condyle bone defects, and betaTCP alone as control into the contralateral femur. We studied two different doses of rhBMP-2 (10 and 40 microg) on two groups of four animals. Evaluation consisted in radiography, histology, and histomorphometry, DEXA, and NMR spectroscopy using an original **method** of quantification. With both doses of rhBMP-2, we observed on radiographs an increase of trabecular bone around implants. Histology showed resorption of the **ceramic**, trabecular bone with osteoblasts and osteoid substance around the implants, and colonization inside the **porous** betaTCP by new bone formed. Histomorphometry showed that the osteoid surface (OS/BS) was greatest with the high dose of rhBMP-2. The difference was slight between the low dose of rhBMP-2 and control. DEXA showed a dose-dependent increase of bone mineral density of rhBMP-2-loaded betaTCP vs. control. NMR spectroscopy confirmed that the amount of new bone formed in betaTCP was greater when betaTCP carried rhBMP-2, and increased with the dose of rhBMP-2 used. We showed that betaTCP was a good matrix for rhBMP-2, which gave it **osteoinductive** properties in an orthotopic site, in a dose-dependent manner. Thus, such composite biomaterial seems to be of great interest in reconstructive bone surgery. Further studies are needed in clinical practice to determine optimal doses.

L23 ANSWER 28 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:274797 BIOSIS
DOCUMENT NUMBER: PREV199900274797
TITLE: Potential of **porous** poly-D,L-lactide-co-glycolide particles as a carrier for recombinant human **bone morphogenetic** protein-2 during osteoinduction in vivo.
AUTHOR(S): Boyan, B. D. [Reprint author]; Lohmann, C. H.; Somers, A.; Niederauer, G. G.; Wozney, J. M.; Dean, D. D.; Carnes, D. L., Jr.; Schwartz, Z.
CORPORATE SOURCE: Department of Orthopaedics, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX,

78284-7774, USA
SOURCE: Journal of Biomedical Materials Research, (July, 1999) Vol. 46, No. 1, pp. 51-59. print.
CODEN: JBMRBG. ISSN: 0021-9304.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jul 1999
Last Updated on STN: 28 Jul 1999

AB Several different biodegradable **bone graft** materials are in clinical or preclinical use for the repair of bone defects in orthopedics, maxillofacial surgery, and periodontics. This study tested the hypothesis that poly-D,L-lactide-co-glycolide **copolymer** (PLG) can be used as an effective carrier of recombinant human **bone morphogenetic** protein-2 (rhBMP-2) and that the composite has **osteoinductive** ability. **Porous** PLG rods were shredded to a particle size ranging from 250 to 850 mum. Active and inactive demineralized freeze-dried **bone allografts** (DFDBA) with a comparable particle size were used as positive and negative controls, respectively. PLG particles were treated with vehicle or with 5 or 20 mug rhBMP-2. DFDBA and PLG particles were placed in gelatin capsules, mixed with vehicle or rhBMP-2, and implanted at intramuscular sites in male Nu/Nu (nude) mice. Each mouse underwent bilateral implantation with implants of the same formulation, resulting in five groups of four mice per group:active DFDBA, inactive DFDBA, PLG, PLG + 5 mug rhBMP-2, and PLG + 20 mug rhBMP-2. After 56 days, the implants were recovered and processed for histology. Bone induction was assessed by use of a semiquantitative scoring system based on the amount of new bone formed in representative histological sections. Histomorphometry was also used to measure the area of new bone formed and the area of residual implant material. The results showed that active DFDBA induced the formation of ossicles containing new bone with bone marrowlike tissue, whereas inactive DFDBA or PLG particles alone did not induce new bone. The addition of rhBMP-2 to PLG particles resulted in new bone formation that had a greater bone induction score than active DFDBA. Moreover, the histomorphometric analysis showed that the addition of rhBMP-2 to PLG particles induced the formation of a greater area of new bone and bone marrowlike tissue than active DFDBA. The resorption of the PLG particles was markedly increased with theaddition of rhBMP-2, suggesting that rhBMP-2 may attract and regulate resorptive cells at the implantation site. The results of the present study indicate that PLG **copolymers** are good carriers for **BMP** and promote the induction of new bone formation. Further, the PLG **copolymers** with rhBMP-2 had a greater effect in inducing new bone formation and resorbing the implanted material than active DFDBA alone.

L23 ANSWER 29 OF 43 MEDLINE on STN
ACCESSION NUMBER: 1999212557 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10196808
TITLE: Current status of **ceramic** coatings for dental implants.
AUTHOR: Lacefield W R
CORPORATE SOURCE: Biomaterials Department, University of Alabama at Birmingham, USA.. blacefld@uab.edu
SOURCE: Implant dentistry, (1998) 7 (4) 315-22. Ref: 21
Journal code: 9206481. ISSN: 1056-6163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English

FILE SEGMENT: Dental Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413

AB There are various **ceramic** coatings available for dental implants. From a commercial standpoint, plasma-sprayed **hydroxyapatite** (HA) is the most popular. These coatings are typically partially amorphous after processing and contain crystalline phases other than HA. Plasma-sprayed HA and the other bioactive **ceramic** coating materials have been shown to enhance bone apposition as compared with uncoated metal implants. Some of the other available materials include the **bioglasses**, other **calcium phosphates** such as fluorapatite and **tricalcium phosphate**, and the inert **ceramics** such as alumina. The plasma-spray process is not optimum for all types of **ceramic** coatings, because it is not suitable for coating **porous** surfaces; the exact control of structure and chemistry is difficult with this process, and bond strength is not as high as is desired for some applications. Alternative **methods** for coating include sol-gel processing, ion beam and radio frequency (RF) sputtering, pulsed laser deposition, hot isostatic pressing, and electrophoretic deposition. The use of **osteoinductive** agents in conjunction with **ceramic**-coated implants is of current interest, and the degree and type of bonding of these agents appear to vary with the composition of the **ceramic** coating. Because there seems to be no satisfactory means of incorporating **osteoinductive** agents into **ceramic** coatings during any of the conventional coating procedures, the best approach seems to be to diffuse the agents into the coating after processing. Other possibilities include the tethering of the agents to the surface of the **ceramic** by suitable organic molecules or the placing of the agent in some carrier material such as a cement, which is placed around the implants.

L23 ANSWER 30 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998376840 EMBASE
TITLE: **Antibiotic**-loaded **porous** **hydroxyapatite** blocks for the treatment of osteomyelitis and postoperative infection: A preliminary report.
AUTHOR: Itokazu M.; Aoki T.; Nonomura H.; Nishimoto Y.; Itoh Y.
CORPORATE SOURCE: Dr. M. Itokazu, Department of Orthopaedic Surgery, Gifu University School of Medicine, 40 Tukasamachi, Gifu 500-8705, Japan
SOURCE: Bulletin: Hospital for Joint Diseases, (1998) 57/3 (125-129).
Refs: 20
ISSN: 0018-5647 CODEN: BHJDEI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Hydroxyapatite** blocks (HAB) can be used to administer **antibiotics** or anticancer drugs because its **porous**

structure allows the gradual administration of the pharmacologic agents. A novel drug delivery system using **hydroxyapatite** blocks was developed for osteomyelitis and postoperative infections occurring after joint replacement. To load the **antibiotics**, **hydroxyapatite** blocks were mixed with an **antibiotic** solution and centrifuged at 1500 rpm for 15 minutes or decompressed in vacuum container at 5 to 10 in. Hg for 20 minutes. Fifteen patients with osteomyelitis including one with tuberculosis and four with infections subsequent to joint replacement were treated with **antibiotic** -loaded **hydroxyapatite** blocks in combination with intravenous injection. Except in one case, all of the foci had completely healed at follow-up (range: 13 to 71 months; average: 39.7 months). These new **methods** are simple and can safely treat osteomyelitis in a one-stage operation.

L23 ANSWER 31 OF 43 MEDLINE on STN
ACCESSION NUMBER: 1998006451 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9348228
TITLE: Modulation of commitment, proliferation, and differentiation of chondrogenic cells in defined culture medium.
AUTHOR: Quarto R; Campanile G; Cancedda R; Dozin B
CORPORATE SOURCE: Laboratorio di Differenziamento Cellulare, Istituto Nazionale per la Ricerca sul Cancro, Centro di Biotechnologie Avanzate, Genova, Italy.
SOURCE: Endocrinology, (1997 Nov) 138 (11) 4966-76. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Space Life Sciences
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971124

AB The factors regulating the growth and development of mesenchymal precursor cells toward chondrogenesis are not well identified. We have developed a defined serum-free culture system that allows the proliferation of chick embryo chondrogenic cells and their maturation toward hypertrophic chondrocytes. Proliferation is obtained in adhesion in medium supplemented with insulin (Ins), Dexamethasone (Dex), and either basic fibroblast **growth factor** (FGF-2), platelet-derived **growth factor** bb, epithelial **growth factor**, or GH; the highest mitogenic response is induced by FGF-2 in synergy with Ins. Ins can be substituted by Ins-like **growth factor** I. When these cells are transferred into suspension culture in Ins/Dex and T3 without **growth factor** supplement, they undergo the complete chondrogenic development characterized by type X collagen synthesis and cellular hypertrophy. During differentiation, Ins cannot be substituted by Ins-like **growth factor** I. Chondrogenesis is also evidenced by the formation of hypertrophic cartilage when the medium is supplemented with ascorbic acid. If T3 is introduced in the proliferation phase, the cells fail to differentiate to hypertrophy in suspension unless **bone morphogenetic** protein-2 is added. Assays of ectopic tissue formation in nude mice, with cells implanted sc after adsorption on collagen sponge or **porous hydroxyapatite ceramics**, indicate that cells grown in Ins/FGF-2 reform mainly cartilage in vivo, whereas expansion in Ins/T3/Dex/FGF-2 leads to the

formation of cartilage, bone, and adipose tissue.

L23 ANSWER 32 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1997:290990 BIOSIS
DOCUMENT NUMBER: PREV199799590193
TITLE: In vitro release kinetics of biologically active transforming **growth factor**-beta-1 from a novel **porous glass** carrier.
AUTHOR(S): Nicoll, Steven B.; Radin, Shulamith; Santos, Eric M.; Tuan, Rocky S.; Ducheyne, Paul [Reprint author]
CORPORATE SOURCE: Dep. Bioeng., Univ. Pennsylvania, Philadelphia, PA 19104, USA
SOURCE: Biomaterials, (1997) Vol. 18, No. 12, pp. 853-859. CODEN: BIMADU. ISSN: 0142-9612.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jul 1997
Last Updated on STN: 9 Jul 1997
AB Sol-gel silica-based **porous glass** (**xerogel**) was used as a novel carrier material for recombinant human transforming **growth factor**-beta-1 (TGF-beta-1). Room temperature synthesis procedures included sol preparation, the addition of TGF-beta-1 solution to the sol, subsequent gelation and drying. After determination of optimal synthesis parameters, the material was assayed in vitro for its ability to release biologically active TGF-beta-1 in a controlled manner. Sustained release of TGF-beta-1 over a 7-day period was demonstrated. On the basis of published TGF-beta-1 potency, the amount released is capable of eliciting bone tissue reactivity. These findings suggest that this novel **glass-growth factor** composite may serve as an effective **bone graft** material for the repair of osseous defects.

L23 ANSWER 33 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1997:290980 BIOSIS
DOCUMENT NUMBER: PREV199799590183
TITLE: Ectopic bone induction in **porous** apatite-wollastonite-containing **glass ceramic** combined with **bone morphogenetic** protein.
AUTHOR(S): Ijiri, S. [Reprint author]; Nakamura, T.; Fujisawa, Y.; Hazama, M.; Komatsudani, S.
CORPORATE SOURCE: Dep. Orthopaedic Surgery, Faculty Med., Kyoto Univ., 54 Kawara-cho, Shogoin, Sakyo-ku, Kyoto 606, Japan
SOURCE: Journal of Biomedical Materials Research, (1997) Vol. 35, No. 4, pp. 421-432. CODEN: JBMRBG. ISSN: 0021-9304.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jul 1997
Last Updated on STN: 9 Jul 1997
AB To accelerate the integration of **ceramic** implants with the surrounding bone and to search for a suitable carrier for **bone morphogenetic** protein (**BMP**), we studied ectopic bone induction in **porous** apatite-wollastonite-containing **glass ceramic** (A-W GC) combined with partially purified bovine **BMP** (bBMP) and recombinant Xenopus **BMP**-4/7 (rxBMP-4/7). **Porous** A-W GC rods (4 mm in diameter, 5 mm in height, 70% porosity, 200 mu-m mean pore size, 17.54 +- 3.82 MPa (mean +-

SD) compressive strength) were used. An apatite coating formed on the surface of **porous** A-W GC that had been immersed in simulated body fluid at 36.5 degree C for 7 days. In experiment 1, **porous** A-W GC rods were combined with either bBMP, collagen, or with both bBMP and collagen. The rods were implanted into subcutaneous pouches in rats and were harvested 4 weeks after implantation. Low-energy radiographic, scanning electron microscopic (SEM), and histological examinations showed ectopic bone formation and within the rods only in the **porous** A-W GC combined with the bBMP and collagen group. Quantitative analysis also revealed that this group alone showed a significant increase in bone formation. In experiment 2, **porous** A-W GC rods were combined with rxBMP and collagen, implanted into rats, and harvested as described above. SEM and histological examination showed ectopic bone formation around and within the rods. Because of its relatively high mechanical strength, ease of handling, and good **osteoinductivity**, **porous** A-W GC combined with **BMP** and collagen may be clinically useful in patients with large cancellous bone defects or craniomaxillofacial lesions.

L23 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1996:55810 BIOSIS
DOCUMENT NUMBER: PREV199698627945
TITLE: Osteoinduction in **porous hydroxyapatite** implanted in heterotopic sites of different animal models.
AUTHOR(S): Ripamonti, Ugo
CORPORATE SOURCE: Med. Res. Council/Univ. Witwatersrand, Bone Res. Lab., Med. Sch., 7 York Rd., Parktown, 2193 Johannesburg, South Africa
SOURCE: Biomaterials, (1996) Vol. 17, No. 1, pp. 31-35. CODEN: BIMADU. ISSN: 0142-9612.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 1996 Last Updated on STN: 10 Feb 1996

AB Previous studies have demonstrated the induction of bone in coral-derived **porous hydroxyapatite** when implanted intramuscularly in baboons. This **hydroxyapatite**-induced bone differentiation model was used to study the effect of different animal species on heterotopic bone formation. **Porous hydroxyapatite**, obtained after hydrothermal conversion of the calcium carbonate exoskeleton of coral (genus Goniopora), was implanted in the rectus abdominis of adult rabbits, dogs and baboons (Papio ursinus). Specimens were harvested on day 90 after implantation and subjected to histological and histomorphometrical analysis. Minimal amounts of bone formed in **hydroxyapatite** specimens harvested from rabbits and dogs. Substantial bone differentiation did occur, however, in **hydroxyapatite** specimens harvested from the rectus abdominis of the baboons. In primates, the **porous hydroxyapatite**, as used in this study, may act as a solid matrix for adsorption, storage and controlled release of circulating or locally produced **bone morphogenetic** proteins, which locally initiate bone formation. The results of this study on heterotopic bone formation in **porous hydroxyapatite** underscore the importance of primate models in biomaterial research, which should be exploited for the formulation of **porous** substrata with intrinsic **osteoinductive** activity.

L23 ANSWER 35 OF 43 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 96114867 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7492710
TITLE: Mechanical properties and histological evaluation of

sintered beta-Ca2P2O7 with Na4P2O7.10H2O addition.
AUTHOR: Lin F H; Lin C C; Lu C M; Liu H C; Sun J S; Wang C Y
CORPORATE SOURCE: Center for Biomedical Engineering, College of Medicine, National Taiwan University, Taipei, ROC.
SOURCE: Biomaterials, (1995 Jul) 16 (10) 793-802.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19970203
Entered Medline: 19960111

AB The ultimate goal of implantation of biomaterials in the skeleton is to reach full integration of the non-living implant with the living bone. The biomaterial can be used much as a **bone graft**, resorbing or dissolving as bone growth occurs, and the end result is a new remoulded bone. **Calcium pyrophosphate**, Ca2P2O7, is one of the intermediate products of bone mineralization. beta-**Dicalcium pyrophosphate** (beta-DCP) doped with certain amounts of Na4P2O7.10H2O was prepared as the developed material. Na4P2O7.10H2O was used as a liquid-phase additive to improve the **sintering** process and promote physiological bioresorbability. Compressive strength and four-point bending strength were measured by the Bionix test system 858. The mechanical strength of the **sintered** beta-DCP increased with the addition of Na4P2O7.10H2O up to 5 wt%, but thereafter decreased. The microstructure and crystal structure were analysed by the **techniques** of SEM, EPMA, TEM and XRD. The relationship between the mechanical strength of the **sintered** **bioceramics** and the Na4P2O7.10H2O dopant was examined in terms of the presence of NaCa(PO3)3, grain growth and abnormal grain coalescence while the dopant increased. Preliminary in vivo evaluation was studied by rabbit femur condyle implantation. There was no **inflammation** or any toxic sign during the experimental period. The histological section of intraosseous implantation revealed that the new bone deposited directly on the surface of the material in the fourth week after operation. The implant gradually decreased in volume and was replaced by the surrounding regenerated bone in the rabbit condyle in vivo environment. The results led us to conclude that the developed material has great potential as a biodegradable bone substitute.

L23 ANSWER 36 OF 43 MEDLINE on STN
ACCESSION NUMBER: 97455118 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9309501
TITLE: Effect of demineralized bone matrix on bone growth within a **porous** HA material: a histologic and histometric study.
AUTHOR: Damien C J; Parsons J R; Prewett A B; Huismans F; Shors E C; Holmes R E
CORPORATE SOURCE: Laboratories for Orthopaedic Research, UMDNJ-New Jersey Medical School, Newark, USA.
SOURCE: Journal of biomaterials applications, (1995 Jan) 9 (3) 275-88.
Journal code: 8813912. ISSN: 0885-3282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711

ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971120

AB Coralline **hydroxyapatite** (cHA) is an osteoconductive material currently being used as a **bone graft** substitute. Created by the hydrothermal conversion of the calcium carbonate skeleton of coral to **hydroxyapatite**, this material has a **porous** structure similar to cancellous bone. Addition of demineralized bone matrix (DBM) would conceivably create a composite with both osteoconductive and **osteoinductive** properties. This pilot study evaluated the healing of rabbit cranial defects that had been filled with cHA or cHA augmented with a DBM gel formed by adding glycerol to the DBM particulate. Data from these were then compared to unfilled defects from a previous study. Results indicated enhancement of new bone formation and an increase in the rate of healing in the defects filled with the cHA-DBM gel composite. Further studies are warranted.

L23 ANSWER 37 OF 43 MEDLINE on STN
ACCESSION NUMBER: 94046147 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8229417
TITLE: Evaluation of new high-performance **calcium polyphosphate bioceramics** as **bone graft** materials.
AUTHOR: Nelson S R; Wolford L M; Lagow R J; Capano P J; Davis W L
CORPORATE SOURCE: Department of Oral and Maxillofacial Surgery, Baylor College of Dentistry, Dallas, TX.
SOURCE: Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons, (1993 Dec) 51 (12) 1363-71. Journal code: 8206428. ISSN: 0278-2391.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Dental Journals; Priority Journals; Space Life Sciences
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19980206
Entered Medline: 19931220

AB The purpose of this study was to evaluate the ability of a recently developed **porous calcium polyphosphate bioceramic** (CPB) to function as a **bone graft** substitute. After six weeks, postsurgical extraction of the mandibular first and second molars, alveolar ostectomies were performed bilaterally in five dogs. The ridge forms were then restored using the CPB implant material on one side and the autogenous bone obtained from the contralateral ostectomy site on the other. The graft and implant sites were retrieved after 4 months and decalcified and undecalcified sections were prepared for special staining (modified Attwood) and subsequent light microscopy and histomorphometry. In addition, the undecalcified sections were prepared for histometry using backscattered electron imaging (BSEI). Histologically, the CPB implants showed extensive vascularization and cellularity within an "invading" loose connective tissue matrix. On the opposite side, the loose connective tissue of the autografts showed hypovascularity and hypocellularity. Neither the implants nor the autografts showed any histologic evidence of an **inflammatory** reaction. Using light microscopic histomorphometry, the implants showed a higher incidence of union than the autografts. On BSEI histometry, the CPB implants showed significantly greater new bone formation than the autografts. This study reveals that **porous** CPB possesses

certain characteristics essential for the "ideal" implantable bone substitute necessary for the repair of craniofacial and other bony defects.

L23 ANSWER 38 OF 43 MEDLINE on STN
ACCESSION NUMBER: 94191585 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8142935
TITLE: **Bone-grafting** materials in implant dentistry.
AUTHOR: Misch C E; Dietsh F
CORPORATE SOURCE: University Oral Implantology Center, Department of Prosthodontics, University of Pittsburgh, School of Dental Medicine, PA 15261.
SOURCE: Implant dentistry, (1993 Fall) 2 (3) 158-67. Ref: 27
Journal code: 9206481. ISSN: 1056-6163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Dental Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940511
Last Updated on STN: 19980206
Entered Medline: 19940505

AB There are three classes of **bone-grafting** materials based upon the mode of action. Autogenous bone is an organic material and forms bone by osteogenesis, osteoinduction, and osteoconduction. Allografts such as demineralized freeze-dried bone are **osteoinductive** and osteoconductive and may be cortical and/or trabecular in nature. Alloplasts such as **hydroxyapatite** and **tricalcium phosphate** may be synthetic or natural, vary in size, and are only osteoconductive. They can be divided into three types based upon the porosity of the product and include dense, **macroporous**, and **microporous** materials. In addition, alloplastic materials may be crystalline or amorphous. These materials have different properties and therefore indications. The use of the three classes of materials in diverse combinations depends upon the size and topography of the bony defect. Small defects or defects with four walls of host bone can be repaired with alloplasts alone or allografts in combination with alloplasts. The loss of three or more bony walls mandates the addition of autogenous bone to the graft or the use of a small pore membrane. The larger the defect, the more autogenous bone is required. The different indications of bone substitutes are discussed as to their specific applications in implant dentistry.

L23 ANSWER 39 OF 43 EMBASE on STN
ACCESSION NUMBER: 92171626 EMBASE
DOCUMENT NUMBER: 1992171626
TITLE: Enhanced osteoinduction by intramuscular grafting of **BMP**-β-TCP compound pellets into murine models.
AUTHOR: Wu C.-H.; Hara K.; Ozawa H.
CORPORATE SOURCE: Department of Periodontology, Niigata Univ. School of Dentistry, Gakko-cho 2-5274,Niigata 951, Japan
SOURCE: Archives of Histology and Cytology, (1992) 55/1 (97-112).
ISSN: 0914-9465 CODEN: AHCYEZ
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology

016 Cancer
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The **osteoinductive** effects of **bone morphogenetic** protein (**BMP**, derived from murine osteosarcoma) were studied with regard to its use combined with β-**tricalcium phosphate** (β-TCP). **BMP** and β-TCP were molded into pellets by the 'pressure **method**', originated by us and transplanted to ddY mice. Control mice received interdorsal muscular implantations of either the **BMP** or β-TCP pellets. The animals were sacrificed 1, 2 and 3 weeks after grafting, for radiological, histochemical, and ultrastructural observations. The **BMP**.beta.-TCP compound pellets induced faster cartilage and bone formation, whereas these activities were slower when pellets made solely of **BMP** were used. The β-TCP pellets demonstrated no **osteoinductive** properties. Observations revealed two types of β-TCP resorbing multinuclear giant cells. One was osteoclastic, expressing calcitonin receptors, having numerous mitochondria and ruffled border-like structures; the other was not osteoclastic in nature. In animals grafted with the compound pellets, a great number of osteoclastic cells gathered on the pellets, much earlier than those grafted with the pellets made of **BMP** alone. Then, osteoblastic bone formation over the cement lines followed an osteoclastic resorption of both β-TCP and newly formed bone. In contrast, **BMP** induced few osteoclastic cells, resulting in slower bone coupling. Furthermore, the faster bone formation induced by the compound pellets seemed to be associated with the presence of β-TCP. **Porous** by nature, β-TCP would entrap **BMP** within its micropores, and thus, the intrinsically diffusible **BMP** is retained and its action consequently prolonged. In addition, the compound pellet offered increased surface contact between **BMP** and mesenchymal cells. Therefore, **BMP**-β-TCP compound pellets induce cartilage and bone formation more rapidly than does **BMP** alone.

L23 ANSWER 40 OF 43 MEDLINE on STN
ACCESSION NUMBER: 92035900 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1934747
TITLE: Interaction of allogeneic demineralized bone matrix and **porous hydroxyapatite bioceramics** in lumbar interbody fusion in rabbits.
AUTHOR: Ragni P; Lindholm T S
CORPORATE SOURCE: Research Laboratory, Orthopaedic Hospital, Invalid Foundation, Helsinki, Finland.
SOURCE: Clinical orthopaedics and related research, (1991 Nov) (272) 292-9.
Journal code: 0075674. ISSN: 0009-921X.
Report No.: NASA-92035900.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Space Life Sciences
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911223
AB Bone repair by autograft is effective in clinical practice. However,

serious problems arise when a considerable volume of transplant is needed, as with spinal fusion procedures. The use of bone substitutes combined with **osteoinductive** agents may contribute to the solution of such problems. In this study, the effectiveness of such a procedure was tested in an experimental model of interbody fusion in rabbits in which the incorporation of a **porous hydroxyapatite** block (HA) was enhanced by the addition of allogeneic demineralized bone matrix (DBM). The latter was used as a delivery system for the **osteoinductive** activity of the **bone morphogenetic** protein contained in the matrix. A group implanted with combined HA + DBM showed significantly earlier stabilization of the fusion when compared to groups implanted with DBM alone, HA alone, and **bone autografts.** On the other hand, the general results of the fusion with HA + DBM were superimposable on those of autografts. With further research, the combination of a bone substitute and an **osteoinductive** agent may constitute an alternative to the use of **bone autografts.**

L23 ANSWER 41 OF 43 MEDLINE on STN
ACCESSION NUMBER: 92231014 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2135110
TITLE: Bone inductive activity of beta-**tricalcium phosphate-bone morphogenetic** protein complex.
AUTHOR: Mieki A
CORPORATE SOURCE: Department of Dental Materials Science, School of Dentistry, Aichi-Gakuin University, Nagoya, Japan.
SOURCE: Aichi Gakuin Daigaku Shigakkai shi, (1990 Mar) 28 (1 Pt 1) 43-58.
Journal code: 7501066. ISSN: 0044-6912.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Dental Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920607
Last Updated on STN: 19980206
Entered Medline: 19920521

AB For the development of new implantable biomaterials as bone substitutes in the treatment of jaw bone defects, **bone morphogenetic** protein (**BMP**) bound to **porous** beta-**tricalcium phosphate** (beta-TCP) was investigated in the present experimental study in mice. The **BMP** was extracted from bovine cortical bone while the beta-TCP was synthesized by a mechanochemical **method.** The affinity of **BMP** to beta-TCP was examined by means of beta-TCP column chromatography. The **porous** beta-TCP combined with the **BMP** by dialysis was implanted in the muscle pouches of mice. The beta-TCP or **BMP** alone was also implanted in the same places in the controls. Three weeks after the implantation a new bone formation was observed in the exterior surface of the beta-TCP/**BMP** complex, but not in that of the beta-TCP control. The quantity of bone induced by the beta-TCP/**BMP** complex was determined on the X-ray film by a computer supported image analysis system. The **osteoinductive** activity of the complex was higher than that of the **BMP** alone. The histological relationship between the beta-TCP/**BMP** complex and the original tissues was excellent. The result of the present study may indicate that the beta-TCP/**BMP** complex can be used as an osteogenetic biomaterial for the treatment of bone tissue defects.

L23 ANSWER 42 OF 43 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 87098612 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3541772
TITLE: Granular **tricalcium phosphate** in large cancellous defects.
AUTHOR: Lange T A; Zerwekh J E; Peek R D; Mooney V; Harrison B H
SOURCE: Annals of clinical and laboratory science, (1986 Nov-Dec) 16 (6) 467-72.
Journal code: 0410247. ISSN: 0091-7370.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198702
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19900302
Entered Medline: 19870205

AB **Tricalcium phosphate** (TCP) is a **porous ceramic** which has biological properties of being non-reactive and resorbable, and acts as a **scaffolding** for bone ingrowth, undergoing progressive degradation and replacement by bone. **Tricalcium phosphate** has been shown to be comparable to autogenous **bone graft** in small periodontal defects. However, orthopedic defects are much larger. This prompted us to review the bone ingrowth potential in large cancellous bone defects (up to 12 cm3) in adult pigs. To quantitate bone ingrowth potential, three skeletally mature pigs had metaphyseal defects created in the tibia and femur of each hind limb, for 12 total sites. Twelve-cc defects in the distal femur and eight cc defects in the proximal tibia were made. Bone curetted was saved to be used as autogenous graft in the control, while the other ipsilateral defect was packed with **tricalcium phosphate.** Four months following the initial defect, the opposite hind extremity was similarly operated. All animals were sacrificed at nine months. Specimens were imbedded in methyl-methacrylate, cut at 120 microns, and stained. The quantity of regenerated bone was measured by histomorphometric **techniques.** Qualitative assessment at four months revealed absence of **inflammation** and TCP surrounded by trabecular bone, which was uniformly viable. There was very little TCP left by nine months. Quantitative analysis revealed the tibias to have a higher percent net bone replacement with TCP as compared to the control (32 percent versus 13 percent). The femoral TCP-filled defects were comparable to autogenous bone (both measured 29 percent).(ABSTRACT TRUNCATED AT 250 WORDS)

L23 ANSWER 43 OF 43 MEDLINE on STN
ACCESSION NUMBER: 84066881 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6645730
TITLE: [Release delay of various **antibiotics** from resorbable **tricalcium phosphate ceramic** granules with soluble coating for local treatment of osteomyelitis. An animal experiment study]. Die Freisetzungsverzogerung verschiedener **Antibiotica** aus resorbierbarem Tricalciumphosphat-Keramikgranulat durch die Verwendung loslicher Uberzuge zur lokalen Behandlung der Osteomyelitis. Eine tierexperimentelle Untersuchung.
AUTHOR: Eitenmuller J; Peters G; Golsong W; Weltin R; Gellissen G; Reichmann W
SOURCE: Langenbecks Archiv fur Chirurgie, (1983) 360 (3) 193-206.
Journal code: 0204167. ISSN: 0023-8236.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198401
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840127

AB The releasing kinetic of **antibiotics** from **tricalcium phosphate** beads was studied in animal experiments. The **porous** TCP-beads were filled with **antibiotics** and coated with biodegradable substances for delaying the release of the **antibiotics.** There were high tissue levels of **antibiotics** in the surrounding bone for many days. This **method** gains an increase in therapeutic safety in treatment of osteomyelitis. The coated TCP-**antibiotic** beads are used simultaneously as **bone graft** and for treatment of the bone infection. There is no need for further operation.

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=> d his ful

     FILE 'REGISTRY' ENTERED AT 17:20:48 ON 18 JAN 2005
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L1             1 SEA ABB=ON  PYRROLIDONE/CN
                  E NMP/CN
L2             1 SEA ABB=ON  NMP/CN
                  E NEP/CN
                  E PB/CN
                  E CP/CN
                  E BMP/CN
L3             2 SEA ABB=ON  BMP/CN
                  E CALCIUM PHOSPHATE/CN
L4             2 SEA ABB=ON  "CALCIUM PHOSPHATE"/CN
                  E HYDROXYAPATITE/CN
L5             1 SEA ABB=ON  HYDROXYAPATITE/CN
                  E SILICA GEL/CN
L6             1 SEA ABB=ON  "SILICA GEL"/CN
                  E XEROGEL/CN
                  E HYDROXYAPATITE/CN
L7             1 SEA ABB=ON  HYDROXYAPATITE/CN
                  E POLYSULFONE/CN
                  E POLYARYLETHERKETONE/CN
                  E POLYOLEFINS/CN

     FILE 'HCAPLUS' ENTERED AT 17:23:33 ON 18 JAN 2005
                  E ?BONE?(W)(?MORPH? OR ?GRAFT?)
L8          7932 SEA ABB=ON  ?BONE?(W)(?MORPH? OR ?GRAFT?)
L9           659 SEA ABB=ON  L8 AND (?CERAMIC? OR ?GLASS? OR ?COPOLYMER?)
L10          282 SEA ABB=ON  L9 AND (?INFLAM? OR ?ANTIBIOT? OR ?ANTIBACT? OR
                  ?BACT? OR ?PARASIT? OR ?FUNG? OR ?VIRAL? OR ?NEOPLAST? OR
                  ?ANALGES? OR ?ANESTHET? OR ?VACCINE? OR CNS OR ?CENTRAL?(W)?NER
                  VOUS? OR ?GROWTH?(W)?FACTOR? OR ?HORMONE? OR ?ANTIHIST? OR
                  ?OSTEOINDUCTIV? OR ?CARDIOVASC? OR ?ULCER?)
L11           15 SEA ABB=ON  L9 AND (?BRONCHODIL? OR ?VASODIL? OR ?BIRTH?(W)?CON
                  TROL? OR ?FERTILITY? OR ?POLYPEPTID?)
L12          284 SEA ABB=ON  L10 OR L11
L13           97 SEA ABB=ON  L12 AND (?SCAFFOLD? OR ?POROUS? OR ?SINTER?)
L14           32 SEA ABB=ON  L13 AND (?METHOD? OR ?TECHNIQ?)
L15           25 SEA ABB=ON  L14 AND ?BONE?(W)?MORPHOGEN?(W)?PROTEIN?
L16           32 SEA ABB=ON  L14 OR L15  32 cits from CA Plus

     FILE 'MEDLINE, BIOSIS, EMBASE, JICST-EPLUS, JAPIO' ENTERED AT 17:30:35 ON
     18 JAN 2005

     FILE 'REGISTRY' ENTERED AT 17:34:09 ON 18 JAN 2005
L17            8 SEA ABB=ON  (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7)

     FILE 'HCAPLUS' ENTERED AT 17:34:25 ON 18 JAN 2005
L18           22 SEA ABB=ON  L16 AND (L17 OR ?PYRROLIDONE? OR NMP OR NEP OR PB
                  OR CP OR BMP OR (?CALCIUM? OR CA)(W)?PHOSPHAT? OR ?HYDROXYAPATI
                  TE? OR ?HYDROXY?(W)?APATITE? OR ?SILICA?(W)GEL? OR ?ANORGANIC?(
                  W)?MINERAL? OR ?XEROGEL? OR ?POLYSULFON? OR ?POLYARYLETHERKETON
                  E? OR ?POLYOLEFIN?)
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L19          193 SEA ABB=ON  L12 AND (L17 OR ?PYRROLIDONE? OR NMP OR NEP OR PB
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                  TE? OR ?HYDROXY?(W)?APATITE? OR ?SILICA?(W)GEL? OR ?ANORGANIC?(
                  W)?MINERAL? OR ?XEROGEL? OR ?POLYSULFON? OR ?POLYARYLETHERKETON
                  E? OR ?POLYOLEFIN?)
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L20 74 SEA ABB=ON L19 AND (?SCAFFOLD? OR ?POROUS? OR ?SINTER?)
L21 22 SEA ABB=ON L20 AND (?METHOD? OR ?TECHNIQ?)

FILE 'MEDLINE, BIOSIS, EMBASE, JICST-EPLUS, JAPIO' ENTERED AT 17:40:17 ON 18 JAN 2005
L22 59 SEA ABB=ON L21
L23 43 DUP REMOV L22 (16 DUPLICATES REMOVED) 43 cits from other databases